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Prevalence and clinical characteristics of primary angle closure in adult Chinese in Liwan District, Guangzhou

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Declaration

I, Mingguang He, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Date: _____

Abstract

Supervisors: Dr Paul J Foster and Professor Peng T Khaw

In 2003, a population survey was carried out in Guangzhou, a large city in southern China, to investigate the prevalence and clinical characteristics of glaucoma in a representative sample of people in one city district. Standard laser iridotomy was performed in one randomly selected eye of the subjects with suspected angle-closure (those with occludable angles but without raised intraocular pressure or peripheral anterior synechiae). Clinical ocular and ultrasound biomicroscopic examination were carried out before and 2 weeks after laser treatment.

Among 1,405 people aged 50 years and over examined (at a 75.3% response rate), crude prevalence of all glaucomatous optic neuropathy was 3.8% (95%CI: 2.8~4.8%), increasing from 1.1% in the 50~59 age group to 5.5% in those aged 70 years and older. The ratio of PACG / POAG cases was 21/29. Prevalences of occludable angles and primary angle closure were found to be 10.2% (95%CI: 8.6~11.8%) and 2.4% (95%CI: 1.6~3.1%) respectively.

Seventy-four subjects in underwent laser iridotomy on one randomly selected eye. The mean IOP before laser was close to the population mean, and fell by an average of 3 mm Hg after laser. Mean ACD, lens thickness and axial length did not change after treatment. UBM quantitative analysis suggested mean drainage angle width increased by 2.6 times in superior quadrant. The iris curvature radius increased from 5.02 mm to 13.31 mm after treatment suggesting marked flattening of the iris. Distance between ciliary body to trabecular meshwork increased from 0.537mm to 0.561mm ($P<0.0001$) suggesting the backward movement of the ciliary body. Iris thickness at 750 micro m location increased after laser suggesting flattening and a reduction of tension on the iris after pupil block had been eradicated.

About one-fifth (14/74) of the treated eyes remained "gonioscopically occludable" even after a patent peripheral iridotomy (PI) had been created. The UBM characteristics of those remaining occludable included: anterior rotation of the ciliary body, angulated or anterior location of the iris insertion and thickening

of peripheral iris.

This study suggests that the prevalence of primary angle closure was comparable to that found in Singapore and Mongolia. Pupil-block was a significant mechanism in 80% of cases of angle-closure.

Statement of Publications

All the studies presented in this thesis were performed by the author. The following publications have been generated directly from the work described within this thesis:

1. He M, Foster PJ, Johnson GJ, Khaw PT. Angle-closure glaucoma in East Asians and European people. Different disease? Eye 2006; 20: 3-12 (Review).

2. He M, Foster PJ, Ge J, Huang W, Zheng Y, Friedman DS, Lee PS, Khaw PT. Prevalence and clinical characteristics of glaucoma in adult Chinese – A population-based study in Liwan District, Guangzhou. Invest Ophthalmol Vis Sci 2006 (In press).

Conference presentation

1. He M, et al. Natural history of angle closure. SNEC-AIGS symposium; Singapore, July, 2004.

2. He M, et al. Prevalence of glaucoma in urban adult Chinese: A population-based study in Liwan District, Guangzhou, China. Paper Session of Glaucoma, the Association of Research and Ophthalmology Annual Meeting, Fort Lauderdale, May, 2005,.

3. He M, et al. Prevalence of glaucoma in urban Adult Chinese: A population based survey in Liwan District, Guangzhou. World Glaucoma Congress, Vienna, July 2005.

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Contents

1. Background

1.1 Primary angle-closure in East Asians

1.1.1 Ethnic origin in East Asia and Chinese

Genetic, anthropological and linguistic studies suggest that early non-homo sapiens populations outside of Africa were completely replaced by modern humans migrating in waves out of north-east Africa. In a recent Chinese Human Genome Diversity Project that involving sampling 28 populations throughout the mainland China, on the basis of the genetic evidence, particularly from a Y-chromosome and mitochondrial DNA data, Lin et al[1] suggested that human settlement in East Asia has occurred in a pattern consistent with this "Out of Africa" hypothesis. Archeological records suggest modern humans migrated into East Asia from the south between 18,000 and 60,000 years age [2]. This was followed by a northward movement following receding glaciers in that area. A southern route also started from mainland Southeast Asia, through Malaysia and Indonesia, eventually continuing eastward to the Pacific Islands. This genetic migration route may suggest the existence of genetic differences between the people living in North and South China.

The majority of the Chinese population consists of Han people (93.3%). Fifty-five official minority nationalities (6.7%), most of whom have their own languages, and are found predominantly in the peripheral regions. The number of "living languages" listed for China is 205. A significant distinction between northern and southern Chinese populations (Han) has been observed in the analyses of genetic markers[3]. More diverse genetic variation was found in southern Chinese compared with northern Chinese. It was believed that this distinction was due simply to the presence of geographical barriers (including the South Transverse Mountains running from Tibetan plateau on the west to the middle China that probably slowed down the migration of modern humans from south to north, but also may perhaps suggest the populations that arrived in China from different sources.

1.1.2 Primary angle-closure glaucoma: Definition and classification

Primary angle-closure glaucoma (PACG) has traditionally been divided into at least 4 clinical types: acute, sub-acute, chronic and latent, based on the

gonioscopic features of the drainage angle, intraocular pressure and symptomatology [4]. However, symptoms appear not to be a good indicator of glaucomatous visual loss: 60-75% of persons suffering an acute episode of PAC recover without optic disc or visual field damage, at least in the short term [5;6]. The majority of Asian people suffering from angle-closure experience no symptoms [7;8] There is a growing trend to adopt a uniform definition of glaucomatous optic neuropathy applying to different mechanisms of disease: open-angle, angle-closure and secondary glaucoma.[9] This was initially intended to standardize the use of the term "glaucoma" in epidemiological research, as signifying visually significant optic neuropathy. The scheme has now been adopted by the American Academy of Ophthalmology [10] and SEAGIG (The South East Asia Glaucoma Interest Group). A classification scheme for staging the disease based on a conceptual model of the natural history of PAC developed by Foster divides angle closure into three stages (**Table 1**).

Table 1. Parallel classification of stage and mechanism of primary angle-closure

Disease staging	
Stage 1	Narrow angle (angle-closure suspect): an anatomical predisposition to closure
Stage 2	Angle closure – partial or total closure of the angle with synechiae and/or raised IOP. This may be divided into: - Non-ischaemic - Ischaemic – with tissue injury such as iris whirling or stromal atrophy, often with a history of symptoms.
Stage 3	Angle-closure with glaucomatous optic neuropathy

This scheme divides people according to stage of disease severity and risk of loss of vision. It does not identify the mechanism that causes the angle to close, and therefore does not guide treatment (it was designed for epidemiological purposes). The mechanisms responsible for angle-closure have been divided into four categories, each abnormality having a more posterior location:

1. Pupil-block
2. Plateau iris
3. Lens-induced
4. Retro-lenticular causes

This mechanistic classification helps to guide management.

1.1.3 Primary angle-closure glaucoma: Incidence and Prevalence

Incidence data is useful in quantifying symptomatic disease. Based on retrospective identification of cases taken from medical records, the incidence of acute PAC in Finland was reported to be 3.8 per 100,000 per year[11], 4.2 per 100,000 per year in Israel[12] and 8.3 per 100,000 per year (95%CI: 5.6-11.0) in Minnesota[13]. These studies all targeted the population aged 30 years and over except 40 years and over in Minnesota. However, they may be criticized on the grounds that they were not prospective, and that case definition was not standardized. A recently published prospective incidence study from Singapore identified a rate of acute PAC of 15.5 per 100,000 per year (95% CI: 13.3~17.7) in the Singaporean Chinese population[14] compared to 7.0 previously in Thailand and 11.4 in Japan after age and sex standardization[15].

Sparse prevalence data suggest that PAC and PACG is uncommon among European-derived people, with prevalence ranging between 0.04% in the Beaver Dam Study[16], 0.1% in Melbourne[17], 0.09% in Wales[18], 0.4% in Baltimore (Oral communication, from J.M. Tielsch, PhD)[19] and 0.6% in North Italy[20]. Again, the differences in diagnostic definition and insufficient power detecting the small prevalence make further comparison difficult.

Reports on prevalence of PAC and PACG in Asia have increased considerably over the last decade. **Table 2** compares studies of prevalence of PAC and PACG in Europeans and East Asians. Studies in Asia, in common with European studies, are of variable quality. Reports from a rural area near Beijing in 1989[21] and Lhasa [22], both suffered methodological drawbacks; angle width was estimated by oblique flashlight test, gonioscopy was not performed for all subjects, and diagnostic criteria and methods were not clearly described. Another population study in Taiwan primarily designed to evaluate screening techniques was compromised by low participation rate[7].

A nation-wide study of glaucoma prevalence in a Japan found a much lower rate of PAC in Japanese, less than 1/3 of the rate seen in Chinese[23]. In 1995, a population-based study of glaucoma prevalence was conducted in Mongolia[8], which found a similar rate of angle closure to Hu's survey in Beijing[21] although the diagnostic criteria differed considerably. In 1997-8, Foster also carried out a

study of glaucoma prevalence in Chinese Singaporeans in the Tanjong Pagar district of the island[24]. When age and gender were standardized, and with identical definitions, the prevalence of angle-closure suspects, angle-closure and PACG was remarkably similar to that seen in Mongolia.

Table 2 Comparison of the published prevalence data on primary angle closure glaucoma in different populations

Study location	N ≥ 40years (Response)	Ratio: PACG:POAG *	Ratio: Symptomatic: asymptomatic	Angle examination §	Diagnostic definitio
Beijing (1989)[21]	3,147 (96.0%)	43:1	34:9	Flashlight Gonioscopy	Angle + IOP Symptom
Japan Nation-wide (1991)[23]	8,126 (50.5%)	28:194 (including 150 NTG)	N/A	Gonioscopy for all	Angle + IOP
Tibet (1992)[22]	1297 (92.4%)	N/A	N/A	Flashlight gonioscopy	Angle + IOP symptom
Taiwan (1996)	562 (10.3%)	N/A	6:11	Gonioscopy for all	Angle + (IOP or D or symptom)
Mongolia (1996)[7]	942 (94.2%)	14:5	3:11	Gonioscopy for all	New ACS/PAC/PA(scheme
Singapore (2000)[24]	1232 (71.8%)	14:22	N/A	Gonioscopy for all	New ACS/PAC/PA scheme
Baltimore (1991)	5308	N/A	N/A	Not described	N/A
Italy (2000)[20]	4297 (73.9%)	N/A	N/A	Screening followed by gonioscopy	(Angle + sympton sign) + (IOP or dis field)

* The ratio shows the actual number of PACG or POAG cases identified.

§Angle-closure was decided by either gonioscopy for all subjects or screening by oblique flashlight test firstly followed by gonioscop

‡ Short abbreviation of the logical connection for diagnostic definition. *Angle*: anterior chamber angle; *IOP*: elevated intraocular pres symptoms of acute episode; *Sign*: PAS or other ischaemic-related iris and lens damage; *DPPT*: Positive dark room provocative test; *Field*: glaucoma visual field damage

† ACS: angle-closure suspect; PAC: primary angle-closure; PACG: primary angle-closure glaucoma. The ACS category includes tho includes those in PACG.

1.2 Assessment methods of anterior chamber configuration

1.2.1 Axial anterior chamber depth

Axial anterior chamber depth (AACD) is probably the most extensively studied risk factor for angle-closure[25-32]. The depth of the anterior chamber is determined by the height of the corneal dome and the position of the anterior lens surface.

1.2.2 Optical measurement

The first attempt to measure the anterior chamber depth was made by focusing on the cornea and then on the pupil border. In 1960s, Lowe reported a new instrument for the optical measurement of ACD by using Haag-Streit optical pachymetry[33]. This instrument uses an image-splitting device and specially designed eyepiece attached to a slit lamp microscope. The image-splitting device divides the image of anterior chamber into an upper and lower half. The upper image is deflectable by rotating the upper plate of the optical pachymeter and the amount of the deflection required to align or to overlap two structures gives and index of the anterior to posterior distance between them. One instrument is used to measure the corneal thickness and the AACD (from corneal epithelium to anterior lens surface). The difference between these two measurements is the real axial anterior chamber depth. This measurement is accurate to 0.05mm. Alsbirk used this method and concluded the error of measurement was ± 0.037mm [34].

Johnson used a photographic system mounted on a slit lamp to measure AACD as well as the anterior chamber volume by using flurescein distribution and photogrammetric method [35;36]. Adjusted by the grid measurement obtained from a standard model eye with known parameters, the three-dimensional image was constructed and measured by the same transparent scale grid. According to this method, the volume of the anterior chamber in 78 normal eyes was estimated to be 0.209 ± 0.037mm^3.

1.2.3 Ultrasound Biometry

Ultrasound has been used to measure the AACD and corneal thickness. This method may be used independently of a slit lamp, and consequently offers a

more portable method of obtaining measurements. One-dimensional "A-mode" biometry (typically at 10 MHz frequency) is the method in most widespread use in ophthalmic practice. A piezoelectric wafer acts as both emitter and receiver for ultrasound waves. Echoes from interfaces of ocular structures such as cornea-aqueous, aqueous-lens, lens-vitreous and the interface between vitreous and inner limiting membrane (ILM) of retina are detected, and converted into distances based on estimates of speed of sound in ocular media. The greater the difference in the two kinds of media property at each interface, the stronger is the echo and the higher is the corresponding spike displayed on an oscilloscope[37]. In a typical ultrasound examination of an eye, there are usually 4 spikes representing the posterior cornea, the anterior and posterior lens surface and the inner limiting membrane of the retina (ILM). The likely range of locations of these interfaces can be specified by setting "gates"- behaving in effect like electronic calipers. Automated detection of peaks between these gates is used to generate measurements for location of various structures. Ultrasound biometry measures the distances based on the velocity and time for the sound transmission. Therefore, most sophisticated biometers usually have several different modes for aphakic, phakic and pseudophakic eyes, because the velocity of the sound is different in these media.

Most commonly, ocular ultrasound is performed using a corneal contact probe, however the stand-off (immersion) technique is also used[37]. Contact biometry (standard handheld pattern) is accomplished by gently placing a probe on the cornea directly in the visual axis. Using a gentle "on and off technique" or mounting the probe on a tonometer set to the intraocular pressure may help to minimize corneal compression[38]. Perpendicularity is judged when all 4 spikes are at maximum amplitude and the retinal spike rises steeply from the baseline at an angle of 90 degrees. The disadvantages of using the tonometer-mounted technique include less flexibility and control over probe positioning as well as a tendency by the patients to converge their eyes when the probe approaches them, causing many scans to be aligned to the optic nerve rather than the macula[39].

The immersion technique of biometry is performed by placing a small waterbath on the sclera, separating the lids[37]. The waterbath is filled with saline or

methycellulose so that the probe can be immersed into the fluid and thus avoids contact with the cornea. The advantage of immersion technique is that it avoids corneal compression and therefore may be more accurate[40;41]. However, immersion technique is more time-consuming and requires equipment software upgrades (to introduce an additional corneal gate).

Measurement errors in ultrasound biometry are, in general, due to corneal compression and misalignment. The amount of compression is probably varied and unpredictable[38]. So, as with the contact technique, the anterior chamber depth should be monitored. It may also be helpful to delete the shallower anterior chamber depth even when the spikes appear to be of high quality. Some ultrasound instruments can monitor the ACD variation and notice those readings with highest variation which are likely not to be reliable. If the alignment of ultrasound is correct, the retinal spike and scleral spike are of similar high amplitude, ideally with retinal spike arising steeply from the baseline. If either the posterior or anterior lens spike is not of high amplitude, the ultrasound beam may be misaligned at an angle through the lens. Misalignment along the optic nerve rather than the macula is identifiable if the scleral spike is absent or not as high in amplitude as the retina spike[37]. There would not be a great difference if the misalignment is toward the optic nerve, but in high myopia eyes with posterior staphylomas or glaucomatous eyes with significant cupping, this difference may become apparent.

1.2.4 Optical Coherence Biometry

Laser partial coherence interferometry (PCI) is a relatively recently developed method of measuring ocular dimensions. Advantages include it being a non-contact technique, elimination of the variability due to corneal compression and the ability to ensure optical alignment towards the true fovea in most cases, thus increasing accuracy. The Zeiss IOLMaster is commercial product using this technology (Zeiss Humphrey System, CA, USA).

IOLMaster is primarily designed for the measurement of axial length and calculating the power of intraocular lenses. It was found to be comparable in lens power calculations with immersion ultrasound biometry[39]. The IOL Master can

also measure anterior chamber depth using the same principles as optical pachymetry. **Figure 1** illustrates the measurement method for the ACD. This measurement was found to be highly reproducible but tended to give deeper ACD values than conventional ultrasound biometry[42-44]. Lam proposed this is because of the ACD were not measured on the axial direction[42].

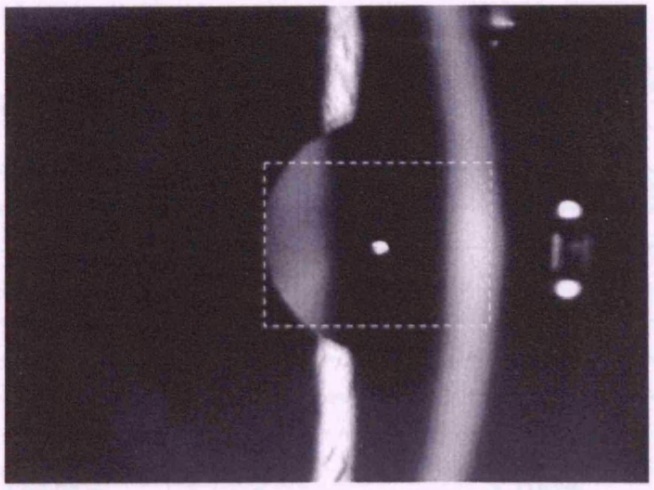


Figure 1 The IOL Master measures ACD using light from a lateral source and a fixation light at the center of pupil.

1.2.5 Limbal anterior chamber depth (LCD)

Estimation of the limbal anterior chamber depth by the van-Herick technique was developed as a non-invasive method for estimating angle width without resorting to gonioscopy. The van Herick technique requires the use of a slit lamp. The illumination column is offset from the axis of the microscope by 60 degrees to the temporal side. A bright, narrow beam of light is directed at the limbus, while making sure that the beam is perpendicular to the ocular surface. A microscope is used to view and grade the limbal chamber depth from the nasal side. The original description outlined a 4 point grading scheme of LCD relative to the adjacent corneal thickness (CT) (**Table 3**). It should be noted that grade 3(1/4~1/2 CT) and grade 4 (>1CT) are not contiguous (i.e. no grade is specified for ½ to 1 CT) [45]. In an attempt to improve the efficacy for differentiating the angle closure in East Asian populations, Foster and Alsbirk proposed a modified scheme with an increased number of subdivisions, and using percentage fractions.[46] The original grade 1 was sub-divided into 0%, 5% and 15% CT, and a grade of 75% CT was added to compensate for the gap between the original

grades 3 and 4. The description of this augmented scheme claimed the cutoff at 15% gave the best combination of sensitivity and specificity in detecting occludable angles (described in the screening section below). Studies show the inter-observer reproducibility for van-Herick test can be good[7;47] although the validity for detecting occludable angles in order to influence long-term prognosis of individuals remains unproven.

Table 3 Original and modified scheme for LCD grading

Traditional van-Herick		**Modified van-Herick**	
----	-----	0% CT	Contact
Grade 1	< 1/4 CT	5% CT	Narrowest possible gap but no contact
---	-----	15% CT	< 1/4
Grade 2	= 1/4 CT	25%	= 1/4
Grade 3	1/4~1/2 CT	40%	> ¼ and < ½
----	----	75%	½ to 1 CT
Grade 4	≥ 1 CT	≥ 100%	> 1 CT

LCD: Limbus chamber depth

CT: corneal thickness

1.2.6 Gonioscopy

Because of total internal reflection, the anterior chamber angle is not visible by routine slit lamp examination alone. By using a contact lens to neutralize the corneal refractive power, it allows either direct or indirect visualization of the angle structures. Troncoso developed the technique in 1925 [48]. It is now routinely used by clinicians to identify different types of glaucoma.

Two gonioscopic techniques have been developed: the direct and indirect methods. A Koeppe lens is an example of a direct gonioscope, and is particularly useful in paediatric patients. The patient can be placed in reclining or supine position. A Koeppe lens is applied after topical anesthesia and methycellulose coupling agent. The examiner uses a handheld microscope with an off-axis light source to view the angle directly. By this method, a non-inverted, non-reversed image of the angle can be seen. The disadvantages are the inconvenience of using the heavy biomicroscope and frequently poor magnification that is

insufficient for optimal observation.

Two styles of mirrored gonioprisms are used for indirect gonioscopy. Both require the use of a slit lamp microscope. The four mirror style typically has a 9mm diameter corneal surface with a radius of curvature (7.72mm) approximately that of the average cornea. Consequently, the lens does not usually require coupling media. Four mirror gonioscopes come in different proprietary versions, such as those with a handle (Zeiss or Posner) or without (Sussman). The presence of four mirrors facilitates rapid examination of the drainage angle throughout a 360° circumference. The angle image is inverted but not reversed. The major advantage of this type of gonioscope is that a dynamic (indentation) examination may be carried out easily. By exerting gentle forward pressure, the examiner can differentiate between appositional (reversible) and permanent synechial closure.[49]

The other category of indirect gonioprism is the *Goldmann* model, which may have one or two mirrors (usually 12mm high and tilted at 28° degrees from the vertical). The corneal surface of these devices has a 12mm diameter and a radius of curvature of 7.38mm. A coupling medium such as methycellulose is required. Goldmann gonioscopes are widely regarded as easier to use than the 4-mirror type, as they permit a clearer, more stable view. Disadvantages include the large diameter and smaller radius of curvature of the corneal surface, which makes a dynamic examination less straight-forward. The use of a coupling medium is not popular with all patients, and many doctors.

Recognition of anatomical landmarks is of paramount important in a gonioscopic examination. Starting posteriorly at the base of the iris, and moving anteriorly, important structures to identify are the ciliary body, the scleral spur, the trabecular meshwork, and Schwalbe's line. Functional (usually pigmented) posterior half of the trabecular meshwork is the most important landmark in identifying closure of the angle. This structure is believed to be responsible for the majority of primary aqueous outflow. If it cannot be seen, the angle is "closed"[50].

During a "static" examination, the angle width is graded in order to make a

prediction of the likelihood of closure. Dynamic or indentation gonioscopy is used to identify peripheral anterior synechiae. Angle width is usually graded and recorded using one of three classification systems, eponymously termed the Scheie, Shaffer and Spaeth schemes.

The Shaffer system is said to be the most widely used in clinical practice.[51] The geometric angle between the corneo-trabecular surface and peripheral third of the iris is estimated. Five categories (recorded in Arabic numbers 0 to 4), represent angles of 0°, 10°, 20°, 20-35° and 45°. However, in clinical practice, it is difficult to assess the angle width in a very accurate and reproducible manner. The Scheie system uses exactly the same number of categories (allocated Roman numerals 0 to IV), describing angle configuration, and the presence of contact between the iris and structures including and surrounding the trabecular meshwork. Grades are allocated according to the visibility of the key anatomical landmarks. A wide open angle is graded "0" (ciliary body band visible), Grade I indicates visibility of the scleral spur, grade III if posterior part of the trabecular meshwork being visible, grade IV represents the narrowest angle with no angle structures are visible. The Spaeth system is the most comprehensive grading system, requiring examiners to identify 4 characteristics of the angle: iris insertion (both apparent and true), angle width, and the iris profile. The iris insertion is assessed as: A- anterior to Schwalbe's line, B- behind Schwalbe's line, C- at scleral spur, D- with narrow, visible ciliary body band, E- very wide ciliary body band. The point of appositional contact between the iris and the posterior surface of the corneo-scleral coat before indentation is recorded as "apparent" iris insertion; while the true point of insertion identified using dynamic gonioscopy is recorded as "real" iris insertion. Geometric angle width is estimated in a similar manner to the Shaffer scheme. Lastly, the iris contour is estimated as: s- Steep or convex, r- regular (flat or with a mild anterior convexity) and q- "queer" or concave. Characteristics of the angle are recorded giving the "apparent" iris insertion, identified using static gonioscopy, in brackets, true level of iris insertion, and assessed using dynamic/indentation gonioscopy, outside brackets. Grades of geometric angle width and iris contour are given subsequently. For example: "(B)D40s" indicates and apparent iris insertion just behind Schwalbe's line, which with indentation is seen to insert into the anterior ciliary body. The angle between the planes of the iris and trabecular meshwork is

40 degrees, and the iris has a steep profile.

The disadvantages of gonioscopy include the dependency on the skill, experience and subjective judgment of examiners. Additionally, configuration of the angle in primary position may be altered by illumination and inappropriate pressure on the gonioscope[52] These may artificially change the appearance of the angle as a result of aqueous redistribution or pupil constriction. Therefore, ideally, during a gonioscopic examination, the room illumination should be as low as possible, the length of slit beam should be 1-2 mm, with a very narrow slit and medium power setting on the slit lamp transformer. Slight tilting of the lens helps when a direct view of the angle is obscured by iris convexity. However, excessive tilting may indent the eye, causing inadvertent pressure to be exerted. This should be avoided, or if absolutely necessary, recognized and the findings viewed in context.

Reproducibility of findings during the gonioscopic examination is another concern when the gonioscopy is used for research purposes. Some authors have cited very good reproducibility[53]. In order to avoid subjectivity of the grading schemes detailed above, Congdon et al proposed the use of an slitlamp eyepiece graticule to measure the distance from iris insertion to Schwalbe's line, termed as "biometric gonioscopy" (BG)[54]. It was claimed BG was significantly correlated with the Spaeth insertion and angle grading system and had similar efficacy in identifying occludable angles, requiring only limited experience of the examiners. Inter-observer agreement between graders without extensive gonioscopic experience showed significantly higher value (kappa=0.97) than routine Spaeth angle grade (0.72) and insertion grade (0.84). As the measurement is based on apparent iris insertion rather than geometric angle, it may be difficult to accurately characterize a closed or significantly narrow angle. This method is yet to gain widespread usage for angle grading.

1.3 Ultrasound biomicroscopy and other anterior segment imaging systems

1.3.1 Overview: Ultrasound biomicroscopy

Ultrasound biomicroscopy (UBM) was firstly developed by Pavlin's group in Canada over 10 years ago [55]. Because it can provide images of the tissues and structures *in vivo* at microscopic resolution, similar to optical biomicroscopy, Pavlin's group termed it "ultrasound biomicroscopy". Instead of using the 10 MHz most widely used in ophthalmic diagnostic ultrasound, UBM uses ultrasound frequencies in the 50-100MHz range, allowing examination of living sub-surface ocular tissues at very high resolution. UBM has found widespread usage as a method of imaging much ocular pathology , from adnexal, conjunctiva, scleral, corneal, anterior chamber to anterior vitreous and retina. However, its major contribution has been to the understanding of the structure of the anterior segment, particularly in glaucoma.

1.3.2 Instrumentation: Ultrasound biomicroscopy

The first clinical model and prototype was developed in the late 1980's, and the first clinical images were taken in March 1990. In cooperation with Pavlin, Zeiss-Humphrey Inc. (San Leandro, CA, USA) developed the first commercial model (Model 840) of the UBM in 1994. Recently, the product line was sold to Paradigm Inc. Additional software has been developed subsequently for image analysis. The newest model (**Figure 2**) is the P45 workstation (Paradigm Ins. US).

Figure 2 The current UBM --- P45 workstation (Paradigm Medical Industries, UT, USA).

A: ultrasound transducer and probe; B: articulated arm; C: computer monitor; D: Main processing unit; E: printer

The development of UBM equipment was made possible by advances in transducer, high-frequency signal processing and precise motion control technology. The principal components of UBM are shown in **Figure 2**. The transducer is the critical component. By moving a transducer linearly over a 5 mm image field, sonographic data are generated along each of 512 lines (8 micron between line) (**Figure 3**). The signal is amplified in proportion to the depth from which it originated using so called "time-gain compensation". After signal processing, ultrasound data can be converted from analog to digital format and transferred to a high speed scan converter, and eventually displayed on a video computer. Only the signals returning from a 5x5 mm area centered at the focal depth are stored. In prototype models, a frequency range of 50-80 MHz with a field of view of 4x4 mm was selected because it can give a useful compromise that allows all the important structures of the anterior segment to be visualized.

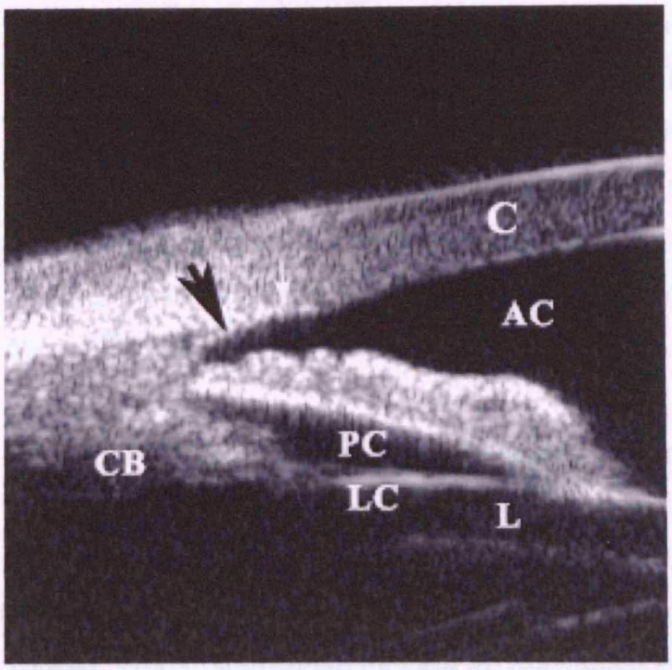


Figure 3 Illustration of major anatomical landmark in UBM images.

(C: cornea; AC: anterior chamber; S: scleral spur; CB: ciliary body; PC: posterior chamber; LC: lens capsule; L: lens). The black arrow shows the most important landmark for drainage angle measurement – scleral spur.

According to the principles of ultrasound physics, image quality is dependent on the frequency of the ultrasound, the ratio of the focal length to the transducer diameter (f-number) and the length of the pulse. Higher frequency and shorter focal length are usually associated with higher resolution of the images but poorer penetration. For example, a device with a high frequency (80 MHzMHz) and short focal length (1.2 mm) can give a very sharp image of the cornea showing the epithelial layer at 50 microns resolution, although the deeper structures of the cornea are not shown clearly.

Measurement accuracy of the imaging system is dependent on the lateral and axial resolution, the stability of mechanical motion, and the pixel size of the image. The lateral resolution (transverse to the direction of pulse propagation) depends on the distribution of ultrasound in the field of the transducer, which has a width at half maximum given by the product of the wavelength and the f-number. Therefore, a transducer of 80 MHzMHz and f 2.2 has poorer resolution than 80 MHzMHz/f1.2. The 80 MHzMHz /f2.2 can capture the resolution of 50 microns. The axial accuracy (resolution) is determined by the speed of sound in the various tissues, for example, 1542 m/s in the iris to 1620 m/s in the sclera.

There are two terms describing the axial accuracy: "instrument axial resolution" and "measurement precision". Instrument axial resolution is the instrument's capability to distinguish two surface when they are brought closer and closer together. "Measurement precision" can be significantly better than axial resolution in some special conditions, such as when the two planar interfaces are well resolved and parallel, e.g., the anterior and posterior surface of the cornea[56].

1.3.3 Examination technique: Ultrasound biomicroscopy

The UBM examination technique is similar to B-mode ultrasound. Transducer direction and manipulation of the probe is guided by looking at the image on the screen. Major differences include an oscillating probe without a covering, the use of a water-bath and the finer movements required.

The patient is examined in a supine position facing the ceiling. After topical anesthesia, a specially-designed eye-cup (22 to 24 mm diameter) is used to separate the eyelids and form a water-bath environment. This is filled with a viscous, sono-lucent coupling fluid Such as methyl-cellulose (1 – 2.5%). Some examiners use normal saline to fill the cup after sealing the interface between the eye and the base of the cup with 2.5% methylcellulose.

Images are stored in an electronic format on a computer attached to the device. This format UBM image files is not compatible with commercially available image editing software. Patient's name, ID number, date of examination and laterality of eye are stored in a separate file. Reviewing images and the derivation of measurements from the images has to be done on the UBM's computer unit or a PC which uses suitable software to process and display the images.

1.3.4 UBM imaging in angle-closure glaucoma

1.3.4.1 Major parameters of UBM imaging in the study of primary angle-closure glaucoma

UBM has proved to be a great asset in the study of angle-closure. Radially-orientated images through the limbus provide a cross-sectional view of

the anterior chamber angle. The corneo-scleral junction and scleral spur can be distinguished in the majority of cases. The scleral spur is usually clearly visible. Quantitative analysis of angle anatomy depends on its accurate localisation. However, in most instances, UBM examination is used for qualitative analysis, such as a confirmation of the angle appositional closure, existence of ciliary rotation or to identify other abnormalities of the ciliary body and angle. Quantitative analysis of the geometric angle width is usually only employed as a research tool.

The quantitative analysis of UBM images in the study of angle-closure usually addresses three specific issues: quantifying the angle width by measurement of either linear distance or geometric angle, and the measurement of area between iris and trabecular meshwork.

Additional measurements of iris thickness and contour as well as the relationship between iris and ciliary body may also be made

A) Angle width quantified by linear distance

As previously discussed, gonioscopic grading depends on the examiner's experience and subjective judgment. The development by Pavlin's group of a UBM method of quantifying angle width in degrees has realized the hopes of many for such a technique [57]. The most commonly used index of angle width is the angle-opening distance (AOD). The scleral spur is identified and a point on the internal wall of the corneo-scleral plane at a given distance from the scleral spur (most often either 250 or 500 microns) is identified. From this point anterior to the scleral spur a line perpendicular to the plane of trabecular surface is extended to meet the surface of the iris (**Figure 4**). The length of this line gives the AOD, termed AOD 250, 500 or 750, dependent on the distance from the scleral spur. AOD at 500 microns was reported to be 347±181 microns in normal eyes [57].

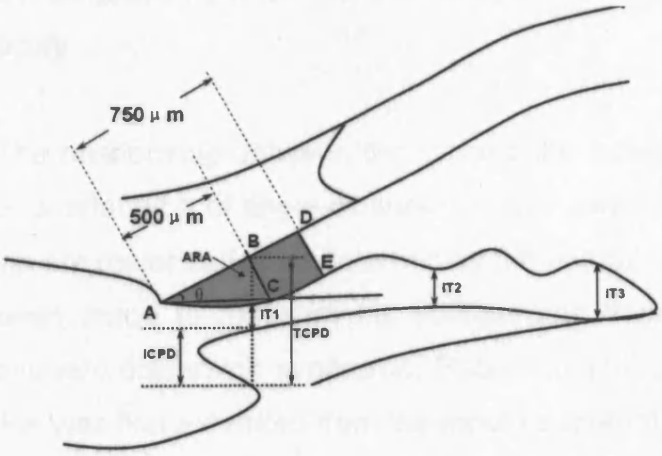


Figure 4 Parameters commonly used for image analysis of UBM. ARA: angle recess area at 750 microns anterior to the scleral spur; IT1-3: Iris thickness at various location to the scleral spur; TCPD: trabecular ciliary process distance; ICPD: iris ciliary process distance.

B) Angle width by degree of angle

Measurement of the angle in degrees (Trabecular-iris angle, TIAθ1) was also proposed by Pavlin, defining the angle as the apex of lines passing through the point on the meshwork 500 microns anterior to the scleral spur and the point on the iris perpendicularly-opposite(Figure 6). However, measurement of the angle using this method was problematic and felt to be of limited validity because of the irregular contour of the iris (**Figure 4**) [57].

C) Angle width by angle recess area

Ritch's group in New York further refined this measurement of the anterior chamber angle. Realizing that all variations in angle anatomy cannot be summarized by either a single measure linear distance or geometric angle because of variations in the contour of the peripheral iris which contribute to the risk of angle closure, Ishikawa developed a parameter called the "Angle recess area (ARA)"[58]. The ARA was defined as the area bordered by the anterior iris surface, corneal endothelium and a line perpendicular to the plane of the corneal endothelium drawn to the iris surface from a point 750 microns anterior to the scleral spur (**Figure 4**).

D) Measurement of iris contour, thickness and relationship with ciliary body

The relationship between the iris and the trabecular meshwork is central to the understanding of angle-closure. Clearly, variation in thickness and shape of the iris are major variables determining the nature of this relationship. Attempts have been made to measure iris contour and thickness by UBM. In the study of pigment dispersion syndrome, Potash described an index of iris concavity[59]. A line was first extended from the most peripheral point to the most central point of the iris pigment epithelium. A perpendicular line is created from this line to the iris pigment epithelium at the point of greatest concavity or convexity Pavlin *et al* proposed that iris thickness measured at 3 locations, perpendicular to the horizontal plane of the iris, the measurements of thickness were made at 500 microns from the scleral spur (ID1), at 2mm from the iris root (ID2), and at the maximum iris thickness near the pupil margin (ID3) (**Figure 4**)

In order to describe the location of the ciliary processes, Pavlin used the trabecular meshwork ciliary process distance (TCPD), measuring this perpendicularly through the iris to opposing body of the ciliary process from a point 500 microns anterior to the scleral spur along the plane of the corneal endothelium (**Figure 4**).

Iris-lens contact distance (ILCD) is another measurement believed to give a measure of pupil block. It is measured along the iris pigment epithelium from the pupil border to the point where the iris physically leaves contact with the anterior surface of the lens (**Figure 4**).

Ishikawa reviewed and illustrated most of these UBM measurements proposed by Pavlin recently as seen in **Table 4**.

Table 4 Parameters proposed by Pavlin and Foster

Parameters	Description
AOD	Distance between the trabecular meshwork and the iris at 500 microns anterior to the scleral spur
TCPD	Distance between the trabecular meshwork and the ciliary process at 500 microns anterior to the scleral spur.
ID1	Iris thickness at 500 microns anterior to the scleral spur
ID2	Iris thickness at 2mm from the iris root
ID3	Maximum iris thickness near the pupil margin
ICPD	Distance between the iris and ciliary process along the line of TCPD
ILCD	Contact between the iris and the lens
TIAθ1	Angle of the angle recess

1.3.4.2 Variation and reproducibility in UBM measurement

Variation in the UBM measurement depends on the image acquisition, image analysis and physiological variability of angle structures. Variation at the stage of image acquisition occurs mainly as a result of inconsistencies in alignment, failure to control accommodation and room illumination. Direction of gaze can be standardized by placing 5 markers on the ceiling to optimize orientation of the eye when measuring different quadrants[60]. However, this method is too time-consuming for use in clinical practice. Standardization of other sources of error is more difficult to achieve.

In order to assess the reproducibility in the quantitative examination using the UBM, Tello calculated interobserver and interobserver variation in measurements[61]. Tello compared image analysis by 3 observers repeatedly measuring the same 4 UBM images. Intraobserver agreement was good in central cornea thickness and anterior chamber depth (Coefficients of variation, CV%< 3.8%) but poorer in angle measurements (CV%1.3%). Interobserver agreement in general was poor and varied considerably, and was thought to be affected by subjective interpretation of location of anatomical landmarks. The TCPD and ID1-3 were less good, while the measurements of AOD and angle width in degrees were the worst.

The authors used "coefficient of variation" (CV) (standard deviation divided by mean) to assess agreement of measurements. However, this index may not be the most appropriate because it assumes the data have a Gaussian distribution. Furthermore, it is probably not appropriate to use this parameter to evaluate the variation in just 3 paired observations. Also, the study suffered from a small number of subjects who all had normal, wide angles, and as a result did not test variation across the entire range of possible values. This limits the extrapolation of the results to eyes with narrow angles which may be more difficult to assess, because of crowding of anatomical landmarks.

Urbak performed a similar study on 50 UBM images obtained by 3 observers. The angle width in these images was not stated in the paper. Using the same statistical methods, the conclusions were similar[60]. Spaeth carried out a more careful evaluation of assessment of angle configuration by UBM[53]. After enrolling 22 patients from his glaucoma clinic, many of them angle-closure patients, he attempted to classify the images by iris insertion, angular width and iris profile, using the same scheme as his (Spaeth's) gonioscopic grading system. Two observers graded the UBM images independently. The intra-observer agreement overall was good with kappa value ranging from 0.83 to 0.92 for the three angle characteristics. The inter-observer agreement was slightly lower for iris insertion (k=0.79) and iris curvature (k=0.84), but measurements of angular width showed remarkably good agreement (k=0.95). This study is the first to demonstrate good intra-observer and inter-observer agreement for UBM images analysis. It also had the advantage that the sample represented a wide range of angle configurations.

It was commonly pointed out that different observers may choose different reference points as the "landmark" for the location of scleral spur and trabecular meshwork outline. There is also the difficulty in measuring exact distances on UBM images. In an attempt to minimize measurement variability, Ishikawa and Ritch developed computer software which calculated AOD and ARA automatically once the scleral spur is identified. This software, UBM Pro 2000, has been made commercially (Paradigm Co)[62]. A new feature was incorporated in the commercial version of this software, which allows AOD to be calculated at

different distances from the scleral spur. Additionally, a regression line is constructed to reflect the iris profile at distances from 250 to 750 microns anterior to the scleral spur (**Figure 5**).

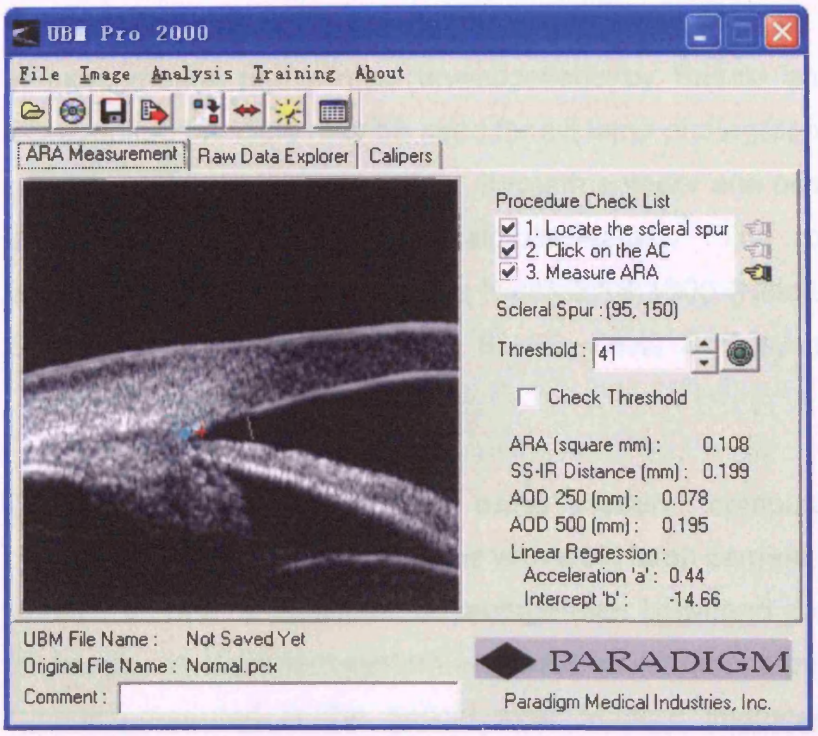


Figure 5 A screen image from the UBM Pro 2000 software package.

1.3.4.3 Contribution of UBM in angle-closure study

UBM provides a unique tool that helps to describe the *in vivo* cross-sectional morphological characteristics of the anterior segment. It can delineate the drainage angle, cross-sectional iris profile, ciliary body, iris insertion, and zone of iris-lens contact, most of which are not visible when using any other ocular biometric devices. In clinical practice, it may help to identify plateau iris, iris crowding and also perhaps longitudinal change of the drainage angle. Limited evidences suggested it can also be used to examine the equatorial zonular region.[63]

1.3.5. Scheimpflug imaging

In order to detect the morphological changes of the crystalline lens *in vivo*, Brown and Niesel introduced the Scheimpflug optical principle into ophthalmology in the 1960s.The technique was refined by Hockwin and applied in experimental and clinical investigations by Sasaki and Dragmorescu The Scheimpflug principle may be used for slit lamp photography of ocular structures, and allowsstructures from cornea, through anterior and posterior capsules of the lens, to be brought into focus simultaneously.[64] The commercial models of Scheimpflug cameras include the Nidek EAS 1000 (Nidek Co., Japan), Topcon SL-45 (Topcon, Japan), Topcon SL-6E, Zeiss SLC system and most recent Oculus Pentacam system.

Obtaining Scheimpflug images using modern, computer-based systems is broadly similar to obtaining images with a slit lamp camera. There is no contact with the cornea- a significant advantage over UBM and gonioscopy. To record a slit image, an alignment system is combined with a computer monitor. A fixation light is presented in the optical axis. Modern instruments typically employ infrared light, with obvious advantages for lens and iris imaging, avoiding light-induced miosis. An image is focused on a screen by moving the computer joy stick. The examiner can freeze a satisfactory image on the monitor, and stored a digital rendition if required. A system for slit beam rotation is included in some instruments, which can be used for image acquisition in different directions and quadrants.

Shibata and Chen used Scheimpflug imaging to measure anterior chamber angles.[65;66] Most commercially available Scheimpflug devices acquire an image that spans limbus to limbus (around 14 mm), allowing the examiner to assess and record images from angles 180 degrees apart.

The process of measurement is aided greatly by image analysis software. The package supplied by the Nidek device requires the examiner to construct a tangent to the most peripheral part of the iris surface, and use a computer pointing device (mouse) to highlight 10 points on the posterior corneal surface. This allows the computer to extrapolate the location of posterior corneal surface.

A tangent to the most peripheral point on the marked corneal surface is automatically extended. The angle between the iris tangent and posterior corneal tangent defines the anterior chamber angle. Using this method in 42 healthy subjects, Chen found there were no inter-quadrant differences of anterior chamber angle width, but there was a significant narrowing of the angle width with age and this age-related trend was greater in women. Reproducibility of this measurement was not reported.

Boker *et al* compared the results of angle biometry obtained from computerized Scheimpflug imaging and UBM.[67] After examining 20 healthy volunteers, and analyzing the images using a "custom windows-based software package" and the UBM measurement method described by Pavlin, it was concluded that Scheimpflug tends to measure a narrower angle width than UBM. The correlation coefficient for the two methods was 0.64. It was also noted that the Scheimpflug camera could not document any structural landmarks in the angle analogous to those seen on gonioscopy) and measurements of the angle are made using an indirect method. Advantages of the Scheimpflug included the fact that it is less invasive (not requiring contact with the ocular surface) and that it was not as time-consuming as the UBM. Again this study was weakened by the fact that it included few eyes with narrow angles. Scheimpflug imaging may offer a means of screening for people at risk of angle-closure, because it is much less invasive and less dependent on the examiners compared with gonioscopy and UBM, if the reproducibility and efficacy in differentiating eyes with narrow angles can be shown to be satisfactory.

1.3.6 Anterior optical coherence tomography

The optical coherence tomography (OCT) technique is a non-invasive high-resolution imaging system which is able to provide *in vivo* cross-sectional images of tissue structures with a spatial resolution of 10-20 microns (about twice as good as UBM). In ophthalmology, the OCT technique has been used predominantly for imaging of the posterior segment of the eye.[68-72] The feasibility of imaging the anterior segment by OCT was first demonstrated in 1994, using a wavelength of 830 nm[71]. It was realized that the major limitation of the system

was limited tissue penetration and failure to image the ciliary body, as a consequence of back-scatter in the sclera, another design employed a wavelength of 1310nm[72]. The scleral backscatter effect of was minimized but penetration was only slightly improved. In ocular tissues, the axial depth of the images was approximately 1.8 mm, with axial resolution of around 15 microns depending on the optical properties. Lateral width of images is variable, up to a maximum of around 7.5 mm. OCT images are displayed either in a logarithmic gray scale or false colors, displaying the reflectivity.

Commercial OCT devices are supplied in a proprietary instrument cowling and operator interface. However, both hand-held and slitlamp-mounted prototypes were designed. The slitlamp-mounted version was found to be easier to operate. Unlike UBM, no water-bath or contact with the ocular surface is required. Acquisition time for a cross-sectional image is variable, ranging from 1 to 4 seconds. However, refinements have made continuous video image capture possible, some models achieving 4 to 32 image frames per second. Significant advantages of OCT for anterior imaging are the feasibility of capturing high resolution, real-time images, without the need for was waterbath or any ocular contact. The technique is particularly suited to the corneal, and to a lesser extent iris, imaging. However, it cannot currently provide useful images of the ciliary body and structures behind the iris because of the high reflectivity of tissues anterior to these. A commercial prototype of an anterior segment OCT has been made by Zeiss, using a 1310 nm laser. Devices are currently undergoing preliminary clinical trials in Europe and the Far East.

1.4 Anatomical characteristics and screening for angle closure

A shallow anterior chamber, short axial length, small corneal diameter and steep curvature, shallow limbal chamber depth, and a thick, relatively anteriorly-positioned lens are all associated with PAC[73].

1.4.1 Anterior chamber depth

Racial difference in the prevalence of PAC appears consistent with the ACD variation in the populations of Greenlandic and Canadian Inuit, Chinese,

Mongolians and European-derived people (Swedes and Americans in Minnesota) [74;75 76 28 31]. **Figure 6** summarizes the relationship between ACD and age in different populations: the lower the mean of ACD, the higher prevalence of PAC in the population. However, Congdon and colleagues have challenged this theory.[77] Using the same protocol for measuring ACD, axial length, radius of corneal curvature and assessing refractive error, Congdon examined 531 Chinese (from a Taiwan population survey with 10% response rate), 170 whites and 188 blacks (from a outpatient clinic in Baltimore) aged 40 years and over. The distribution of ACD and axial length were not significantly different in these 3 ethnic groups. The only difference was smaller radius of corneal curvature in Chinese eyes. Thus, Congdon suggested that mechanisms other than pupil-block (and associated with a shallow anterior chamber) are responsible for the proportionally higher rates of PACG in Chinese people. Terms such as "plateau iris" and "creeping angle-closure" were cited as possible causes. However, several weaknesses, including the low participation rate in the Taiwanese cohort, possibly resulting in selection bias, make it difficult to view the objections raised as incontrovertible. For instance, selection bias may have resulted in more myopic subjects being enrolled, thus distorting the distribution of ACD. Measurement errors attributable to the handheld ultrasound technique might also have affected the validity of ACD measurements.

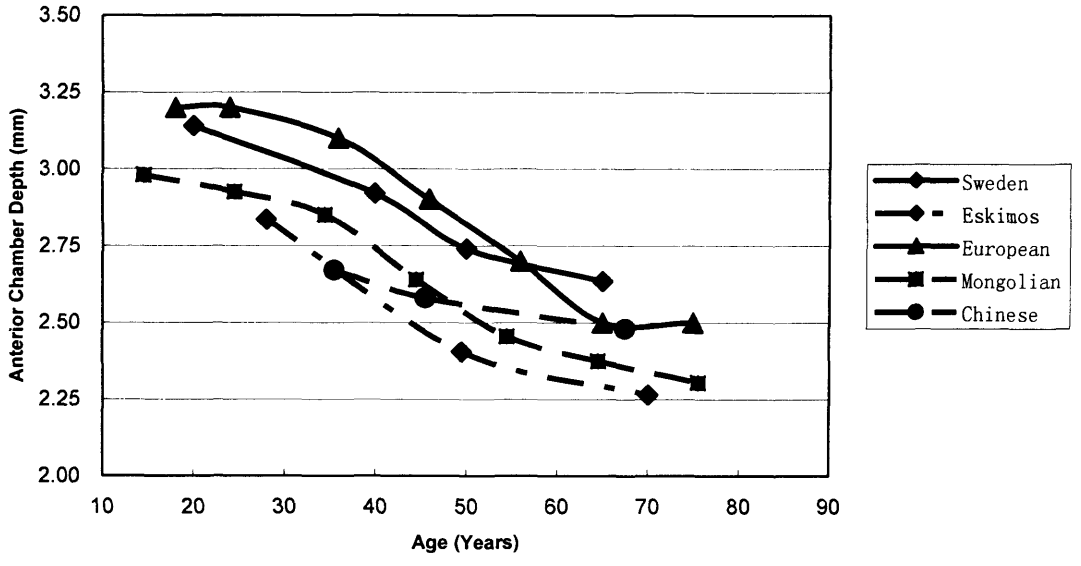


Figure 6 Racial difference in anterior chamber depth

Alsbirk examined the distribution of ACD in a population of Greenland Eskimos.[78] Comparing ACD measured by optical pachymetry in 60 people with PAC and PACG, with that of 1072 people drawn from the population at large, mean ACD in PAC and PACG was 0.5mm shallower. The author also pointed out that this difference in ACD between the unaffected and established cases in Eskimos was smaller than in Caucasians. In another study of 505 adult Greenland Eskimos, Alsbirk pointed out that finding people with an ACD < 2.0 mm would identify those with a gonioscopically narrow angle with the best efficacy. Devereux and colleagues provided a comprehensive evaluation of ACD measurements in a Mongolian population.[38] ACDs measured by optical pachymetry, slitlamp-mounted and handheld ultrasound were compared in their ability to detect occludable angles, PAC and PACG. The area under a receiver operating characteristic (ROC) curve was used as an index of test performance. This graphical technique was originally developed to assess signal-to-noise ratio in radar detection of aircraft. False positive error rate (1-specificity) is plotted on the x-axis, against sensitivity on the y-axis. Consequently, the graph gives an illustration of likelihood ratio of a positive diagnosis. In Devereux's report, optical pachymetry performed better than ultrasound, while the use of a slitlamp mounted ultrasound probe and handheld ultrasound did not differ significantly in screening efficacy. A cut-off value 2.22mm in optical pachymetry ACD was identified to give sensitivity 85% and specificity 84% in detecting eyes with gonioscopically occludable angles. The same paper summarized other published reports of methods of screening for angle-closure. Alsbirk's report on Eskimos found the best segregation between affected and unaffected people was achieved by using an ACD of 2.00mm as a cut-off. This was a little shallower than in the Mongolian population (2.20mm), and may be explained by the smaller mean ACD value in Eskimos.

Table 5 Efficacy of using ACD as screening tools in identification of angle closure

	Alsbirk	Olurin	Congdon	Devereux	Devereux	Devereux
Location	Greenland	Nigeria	Taiwan	Mongolia	Mongolia	Mongolia
Setting	Community	Clinic	Community	Community	Community	Community
No. of Subjects	1067	289	562	1717	937	461
Test	Optical	Optical	Ultrasound	Optical	Slit lamp Ultrasound	HH ultrasound
Cutoff,mm	<2.00	<3.00	<2.70	<2.20	<2.60	<2.53
Sensitivity	88 (38/44)	59(74/126)	77(10/13)	85(109/129)	83(52/63)	86(44/51)
Specificity	88 (897/1023)	61(100/163)	87(427/491)	84(1271/1518)	81(703/872)	73(296/404)
Criteria	Symptoms Tonometry and gonioscopy	No specific criteria	Gonioscopy (180 degree)	Gonioscopy (270 degree)	Gonioscopy (270 degree)	Gonioscopy (270 degree)

1.4.2 Limbal anterior chamber depth

Limbal anterior chamber depth (LACD) estimation was proposed as a screening method to estimate the anterior chamber angle width by van Herick and subsequently used in the population studies in Framingham[79] , Mongolia[46], Greenland[25], Rotterdam[80], North Italy[20] and the Tibet Eye Study [22;22]. **Figure 7** summarizes the percentage of eyes graded as <25% ("Grade 1") of the peripheral corneal thickness (PCT) according to age in several different population studies. The percentage of eyes with LACD $\leq$ 25% (including "Grade 2") of PCT was 1.3% in Tibetans, compared with 6.9% in Beijing Chinese (age-specific percentages were not given in the articles). In general, the van Herick method indicates the limbal chamber tends to be shallower in the Sino-Mongoloid populations compared with Europeans. Surprisingly, the limbal ACD in Japanese is closer to and a little deeper than in European eyes.[23]

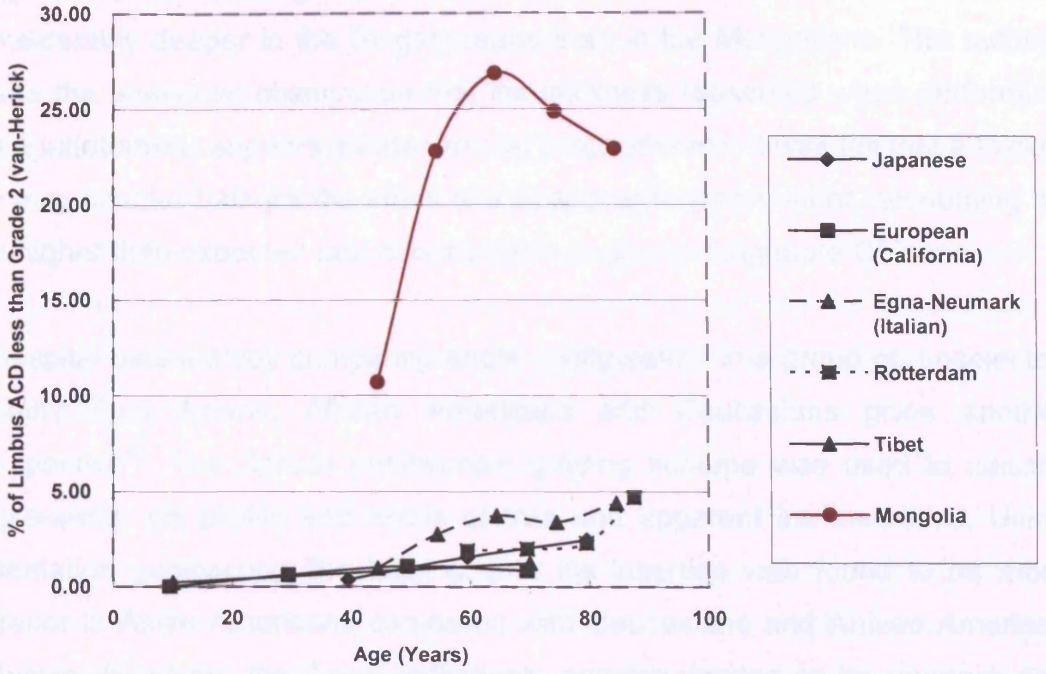


Figure 7 Limbal chamber depth distribution across studies from Japan[23], California, Egna-Neumark (Italian) [20], Rotterdam[80], Tibet [22] and Mongolia[46].

1.4.3 Gonioscopy

There have been few reports of gonioscopic characteristics in population studies: Framingham[79], Mongolia[8], Singaporean Chinese[24] and Cape-Malay people in South Africa[81]. There have been more reports of gonioscopic examinations from clinic-based studies. Of particular interest is a report of Vietnamese people in the USA[82], and a comparison of African, Chinese and European Americans[83]. From these studies, racial differences in gonioscopic findings become apparent: the proportion of narrow angles (i.e. Shaffer Grade≤2), was found to be only 3.8% among European Americans in the Framingham study, and as high as 48% (8.5% with grade 0 or 1 angles) in a group of Vietnamese patients of the same age enrolled from an ophthalmic clinic. However, variations in completeness of details on subject selection and examination protocol preclude a precise comparison. Salmon identified Shaffer grade 1 angles in 9% of subjects from a total of 987 people (40 years and over) of mixed ethnicity from the Western Cape region of South Africa.[81] Using an identical definition of an "occludable" angle to that used by Salmon, studies in Mongolia and Singapore found occludable angles in 6.4% (95%CI: 4.3-8.5) and 6.3% (95%CI: 4.9-7.6) of the populations

respectively. One incongruity noted in these studies was that mean ACD was considerably deeper in the Singaporeans than in the Mongolians. The authors made the anecdotal observation that iris thickness (observed when performing laser iridotomies) appears greater among Singaporeans. It was felt that a thicker iris may counter-balance the effect of a deeper anterior chamber, accounting for the higher than expected rate of occludable angles in Singapore Chinese.

A hospital-based study comparing angle configuration in a group of, unselected healthy East Asians, African Americans and Caucasians gives another perspective[83]. The Spaeth gonioscopic grading scheme was used to classify angle-width, iris profile and levels of true and apparent iris insertions. Using indentation gonioscopy, the level of true iris insertion was found to be more anterior in Asian Americans compared with Caucasians and African American subjects. However, the Asian individuals enrolled tended to be younger and more myopic (and presumably had wider angles). It was proposed that this characteristic may increase the risk of PAS formation in Asian eyes. Members of the same research team using biometric gonioscopy (BG) identified no significant difference (in BG units) between Singaporean Chinese, and African and Europeans Americans in Baltimore after matching the age and sex. However, the Chinese subjects appeared to have wider angles when young and significantly narrower angles in older age compared with Americans. This resulted in similar mean angle widths but significant age-related narrowing of the angle in elderly Chinese[84].

1.5 Mechanism of angle-closure

1.5.1 Appositional and synechiae angle closure: common pathway

In 1938, Barkan first described peripheral anterior synechiae between the peripheral iris and trabecular meshwork that could lead to rising intraocular pressure. In the 1960s, Gorin gave two descriptions of the mode of closure based on his gonioscopic observations[85]. The first phenomenon was that there was appositional contact between Schwalbe's line and the peripheral iris, followed by the formation of PAS in an anterior-to-posterior direction. Secondly, he suggested, PAS may form initially in the periphery of the angle and then

progress toward the Schwalbe line in a posterior-to-anterior fashion that was termed as "shortening of the angle". Subsequently, Lowe coined the phrase "creeping" angle-closure to describe closure in asymptomatic cases, and suggested that synechial closure of the angle occurred gradually in an posterior-anterior and circumferential direction[86]. PAS formation was also described in other secondary glaucomas, such as neovascular or iridocorneal endothelial syndrome (ICE) glaucoma. Synechiae secondary to the formation and contraction of the membrane between the iris and the trabecular meshwork was suggested.

The pattern of angle-closure and distribution of synechiae in PAC were also described by several studies, after comparing the acute and chronic type of PAC, based on the findings by gonioscopy. Phillips found the PAS formed in the superior half of the angle in individuals without symptoms and suggested the PAS progress to the nasal and temporal sectors as ageing increase of lens thickness[87]. A similar study in Indians eyes using dynamic gonioscopy assessed the PAS in 171 eyes of 101 people with PAC. The morphology of PAS was found to differ according to the clinical types of PAC: narrow PAS were most common (53%) in chronic cases, while broad PAS (74%) appeared most common in acute cases. Broad PAS in acute PAC were more likely to be in the quadrant where iris ischaemia was noted.[88] In Chinese eyes, Sun described a similar pattern of PAS in asymptomatic PAC.[89] Sun also observed that there are scattered "crests" on the surface of last roll of peripheral iris which might eventually become the initial point of contact in formation of the spine-shaped PAS in the superior and nasal quadrant. It was suggested that these adhesions would subsequently extend and merge as the diseases progressed.

However, most studies deal with morphological observation, while the pathogenic mechanism for PAS formation remained poorly understood.

1.5.2 Pupil block mechanism

Pupil block is believed to be the major causative mechanism in most cases of angle closure in the West. Chandler[90] and Lowe[91] suggested pupil block is the consequence of contact between iris and anterior lens surface of the lens, and is

exacerbated when the anterior lens surface lies anterior to the plane of the iris root. This contact increases the resistance to aqueous passing through the pupil region from posterior to anterior chambers. In 1964, Lowe proposed a more sophisticated "vector" model of pupil block, describing a conceptual resultant vector from co-contraction of both sphincter and dilator muscles.[86] Using pharmacological provocation tests and anterior segment photographs, Mapstone refined this vector model of pupil blocking force, proposing it resulted from three forces- sphincter and dilator muscles, as well as iris elasticity, which was further enhanced by forward movement of lens-iris diaphragm (**Figure 8**). Together, these three generate a resultant force perpendicular to the lens surface, causing relative or absolute obstruction to aqueous flow.[92] In eyes with PAC, the unique anatomical configuration (anterior position of the lens causing a shallow anterior chamber) decreases the angle between the respective vectors, increasing the resultant force onto the lens surface, and exacerbating relative pupil block. The pupil blocking force then precipitates a resistance to aqueous flow from posterior to anterior chambers. This then generates a pressure gradient across the iris, causing it to bow anteriorly.

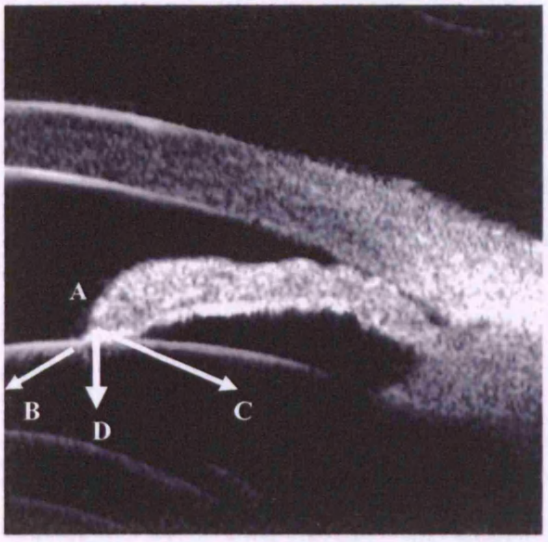


Figure 8 UBM images for primary angle closure suspect eyes with a predominant pupil block mechanism. A-B: vector due to contraction of sphincter muscles; A-C: vector of both dilator muscles and iris elasticity; A-D: resultant vector perpendicular to the lens surface.

1.5.3 Plateau iris configuration

Observations of the effects of PI and UBM imaging of the drainage angle

suggest that the pupil block hypothesis alone cannot satisfactorily explain all cases of angle closure. The term "plateau iris" is often, and some believe incorrectly, used as an umbrella term for all cases of angle-closure where pupil-block has theoretically been eradicated by an iridotomy. More correctly, it is a term that describes both a particular configuration of the peripheral iris, and a syndrome characterized by angle-closure occurring in an eye with a patent iridotomy and plateau iris configuration. This configuration of the peripheral iris in many Europeans is caused by anteriorly positioned ciliary processes that rotate and push the peripheral iris forward, resulting in the characteristic very abrupt change in profile of the peripheral iris, when the central iris has a relatively flat contour (**Figure 9**). Typically, this is seen to be associated with an absent ciliary body sulcus on UBM imaging. The term "plateau iris" was first coined by Tornquist[93] and gonioscopic features of plateau iris described by Wand[94]. UBM imaging has helped clarify the contributions of various anatomical characteristics that are responsible for this clinical entity[95;95;96].

Plateau iris *syndrome* is recognized as episodic or persistent angle-closure after iridotomy. PI alone is ineffective in preventing angle-closure in "pure" plateau iris. The risk of closure depends on the proximity of the peripheral iris to the trabecular meshwork, and exposure to predisposing factors such as pharmacological dilation of the pupil. Rich suggested the height of the plateau as the major determinant of the risk of angle closure, also pointed out the gap between trabecular meshwork and ciliary process and the iris insertion are also important.

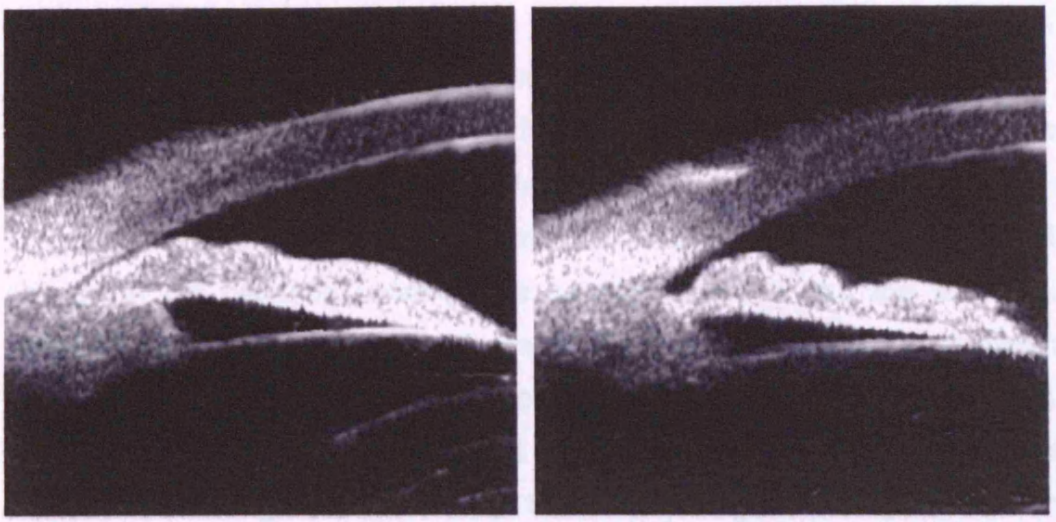


Figure 9: UBM images of plateau iris configuration (left: typical plateau configuration, Right: atypical plateau configuration: Sources: From the image database of the study in Liwan District.

The detection of plateau iris configuration relies on gonioscopy and/or UBM examination, while the confirmation of plateau iris syndrome usually has to be made by observing the drainage angle change after a patent iridotomy has been created.

The natural history of plateau iris syndrome is poorly understood, in part because it is quite an uncommon disease in the European eyes. The clinical signs of plateau iris syndrome are believed to be similar to other angle-closure caused by pupil block: some cases may become symptomatic and present with pain, redness and blurred vision. In the asymptomatic, chronic form it is characterized by gradually increasing IOP and visual field loss. In Lowe and Ritch's textbook, plateau iris syndrome was divided into "complete" and "incomplete" forms, depending on whether the IOP rises are a presenting feature[97]. Ritch proposed that if the plateau rises to the level of the upper trabecular meshwork or Schwalbe line, IOP rises may occur (complete form). Such IOP rises would often accompany pupil dilation. On the other hand, in the incomplete form, peripheral anterior synechiae form over time with continued appositional closure. Therefore, the incomplete variety will typically present as asymptomatic angle-closure.

As stated previously, typical plateau iris configuration, with an angulated peripheral iris, is widely believed to occur because of anteriorly rotated ciliary

process. The reason for the anterior rotation remains unknown. It is uncertain whether this is inherited or acquired. The inheritance theory proposed the absence of a ciliary sulcus is due to failure of the ciliary processes to separate from the posterior iris surface during embryogenesis.[98] A competing theory suggests the configuration may result as a consequence of an "acquired" change in the distance between the zonular insertion and the lens equator increases with age. This eventually leads an anterior shift of the zonular ligament, thus suggesting the anterior movement of the ciliary body is secondary to the traction and anterior displacement of zonular apparatus. Another explanation proposed is a congenital variation in the point of origin of the posterior zonular fibers, leading to a change in ciliary body morphology. This is used as an explanation for the occurrence of plateau iris in younger patients. However, a recent UBM study by Ritch and his team found the iridociliary apposition (absence of ciliary body sulcus) persists even after cataract extraction, which seems to disprove the hypothesis of an association between a zonular anomaly and plateau iris configuration.

Pavlin investigated anterior segment changes in plateau iris syndrome associated with dark, light and pilocarpine administration.[99] In 10 eyes of 10 patients, they found the distance between ciliary processes and trabecular meshwork (TCPD) did not change significantly from dark to light, or with pilocarpine administration, suggesting the increase in angle width was solely because of a reduction in iris thickness. Conceptually, the distance between ciliary processes and trabecular meshwork comprises iris and the width of the aqueous-filled space of the drainage angle. However, they noted that the dimensions of the TCPD remained unchanged in different illumination conditions and with exposure to pilocarpine. This observation further confirmed that support from the ciliary body on the back of peripheral iris is the major factor preventing a flattening of the peripheral iris contour after iridotomy.

Long-term use of miotic agents, peripheral iridoplasty and filtration surgery are all suggested as useful treatments, but these are not uniformly effective in every patient. The proportion and contribution of plateau iris configuration/syndrome in angle closure is unknown, which hinders the planning of effective screening and treatment strategies for PAC, particularly in the setting of a high risk population.

1.5.4 "Prominent last iris roll"

"Prominent last iris roll" and "peripheral angle crowding" are two other terms used to describe non-pupil block entities which perhaps refer to the same characteristics. Although a quantitative comparison has not been made, anecdotally the thick, dark brown iris of Asian eyes occupies a larger proportion of anterior chamber volume than a thin blue iris. With dilation of the pupil, the peripheral iris becomes even thicker often with the formation of one or more circumferential folds. These may come into contact with the trabecular meshwork and lead to appositional closure.

1.5.5 Mixed and other mechanism

In East Asians, mixed mechanism disease (the co-existence of pupil block and non-pupil block) is considered important.[100] In 126 cases of primary angle closure glaucoma (diagnosis: 58 acute, 68 chronic), Wang N in China reported the proportions of pure pupil block, pure non-pupil block with anterior rotation of ciliary body, pure non-pupil block with peripheral iris crowding, combined mechanism were 38.1%, 4.0%, 3.2% and 54.8% respectively. The mechanism classification was based on UBM images: pure pupil block if angle-closure was exclusively due to convexity of the posterior surface of the iris, pure non-pupil block if posterior surface of the iris is flat (this category was further classified into type of anterior rotation of ciliary body and thickening of peripheral iris), combined mechanism of both the features of pupil-block and non-pupil co-existing[100]. .However, the subjects of this study were all from a hospital clinic, and presumably suffered multiple or complex pathology. Subjects included cases of previous acute angle-closure and people with chronic angle-closure. However, an analysis comparing these two sub-groups was not conducted. Furthermore, these two diseases entities represented a small proportion of all cases in the population, while primary angle-closure suspects, the largest group in the population, were not carefully assessed. An examination of mechanisms of angle-closure in representative members of a population outside hospital would give a clearer idea of the true prevalence and impact of angle-closure diseases. This information would have greater validity for developing public

health strategy.

Two strategies are commonly employed to quantify the contribution of pupil block,. One is the study on the effect of PI, identifying "post-iridotomy angle closure". Second is the study of provocative testing,[101] on the basis that angle-closure can be exacerbated by a prone posture, darkness or by use of pharmacological agents.[92]

1.5.6 Cilio-lenticular block and force from posterior segment

The anatomical and functional dynamics of the cilio-lenticular and zonular region are not fully understood. Methods of examining this region include ultrasound and MRI. Most cases of cilio-lenticular block are secondary to other pathological processes, and are usually grouped together as malignant glaucoma. The cardinal signs of "malignant glaucoma" are a shallow axial anterior chamber and high IOP. The anatomical basis of these signs is believed to be contact between the ciliary body and the lens equator, leading to a posterior diversion of aqueous flow. These circumstances usually occur following the use of strong miotic agents or after glaucoma filtration surgery. In classic phakic malignant glaucoma, Pavlin observed the existence of a supraciliary effusion on UBM. He suggested this was induced by a period of hypotony or over-filtration causing a small rotation of ciliary body[102].

Uveal effusion, or idiopathic choroidal expansion, has been suggested as a predisposing factor for angle-closure. Pharmacological agents inducing choroidal expansion, such as topiramate, are known to cause angle closure.[103] The uveal expansion is also assumed to be another mechanism for anterior movement of the lens in primary PAC, aggravating pupil block.[104] The author developed this hypothesis from the observation of the posterior pressure during cataract surgery in PAC cases.

1.6 Natural History

In the early stages, elevation of the IOP in PAC is due to the pre-trabecular meshwork obstruction by the peripheral iris. In the later stages, trabecular

damage and PAS formation are probably responsible for long term pressure elevation. A multi-centre study in North America suggested some degree of angle-closure developed in 25 out of 129 (19%) individuals with central ACD ≤ 2.0 or with an "at risk" angle decided by experienced specialists (this was not defined) after an average interval of 2.7 years[105]. Among Greenland Inuit, Alsbirk found 12 cases of PAC (termed acute (5), intermittent (3) or latent(4)) in 75 people with van Herick limbal chamber depth grade 0-2, or a central ACD < 2.70mm, equal to 16% in 10 years[106].

Thomas and his colleagues examined a relatively young cohort of 50 PACS subjects (mean age: 54.8 years) enrolled from a population-based study 5 years after an initial examination in Vellore, south India.[107] They identified 11 (22%, 95%CI: 9.80 to 34.2) subjects progressing to PAC (11 developed synechial PAC, 4 developed appositional PAC with elevated IOP > 21 mmHg), but none developed a symptomatic episode, and none developed PACG (with either either structural or functional evidence of glaucoma). Based on the the absence of direct progression to PACG, and the current cataract campaign in India, the authors questioned the justification for large-scale prophylactic treatment of PACS subjects. The authors also examined the progression from PAC to PACG in the same population study.[108] Among 28 PAC subjects, 8 (28.5%) progressed to glaucoma. These progression rates were similar in subjects with either synechial or appositional closure. Only 9 had undergone laser PI when they were found to have PAC (although this was recommended in all cases. There were no ocular biometric indices (axial length, ACD and lens thickness) found to be associated with progression from PACS to PAC, or from PAC to PACG. However, gonioscopic findings in this study were not documented carefully at baseline (dichotomously recorded: pigmented TM seen for >/=180 degree or not). This drawback hindered a more meaningful investigation of the mechanisms of angle-closure responsible for progression. Other drawbacks included a small number of subjects and the relatively young age of the sample.

1.7 Provocative testing

Provocative tests are intended to simulate the physiological conditions under which angle-closure may occur. The outcome measure used to assess if this

does happen is a rise in IOP of 8 mm Hg. . The purpose of provocative tests is to differentiate between those cases requiring further intervention, and those that can safely be observed. Provocative tests used commonly in clinical practice are listed below:

1. Dark room test (1910)
2. Moving picture (cinema) test (1930)
3. Reading test (1955)
4. Triple (cycloplegic/water-dringking/pilocarpine) test (1965)
5. Prone test (1968)
6. Dark room prone test (1972)
7. Mydriatic test
8. Pilocarpine-phenylephrine test (1981)
9. Positional pilocarpine test (1981)

Dark room test is firstly described in details by Higgit in 1954[109]. It is performed by measuring the change of IOP before and after the patients sits (remaining awake) in a dark room for one hour. In Higgit's study, the average rise of 2.1 mmHg was found in normal eyes and 16.2 mmHg in eyes with "congestive glaucoma". Foulds observed the pressure elevation of more than 8.6 mmHg would occur in normal eyes only by 1%, and therefore suggesting this as the cut-off for identifying narrow angle eyes at risk for angle closure.

The moving picture or "cinema" test was suggested after it was observed that some patients complained of eye pain or blurring after visiting the cinema. However, this test is probably best interpreted as a component of the history of the presenting complaint, and is not used in PAC diagnosis on the ground of the significant variation in results.

The reading test was first proposed by Higgit following observations of two 2 young patients [110]. Both patients had plateau iris configuration on gonioscopic examination, normal IOP and a negative dark room test. The IOP increased to 40-65 mm Hg after reading for 20-30 minutes. The suggested mechanism for IOP elevation was contraction of the ciliary ring and subsequent rotation of the ciliary body during sustained accommodation. The author suggested pupil block was not important in these cases and in fact pupil block might become less

during reading because of the miosis. Again, this was only based on very few sporadic cases, and there is no evidence that it is useful in predicting= angle-closure in larger groups of individuals.

Hyams devised the prone provocative test, performed by having patients lie face down for about one hour, without putting pressure on the eyes or going to sleep. An IOP rise of more than 8 mmHg was considered positive.[111] It was felt that the mechanism was enhanced pupil block, as a result of forward movement of the lens relative to the iris. Among 82 eyes with definite or suspected angle closure, 25 had positive prone test and negative dark room test. Only 6 eyes had a positive dark-room test and a negative prone test. Less than 5% of eyes with POAG or normal control eyes showed positive result in prone test, all of which may suggest prone provocative test is more sensitive for identifying people susceptible to exaggerated pupil block. In an attempt to increase the predictive value of the test, the prone darkroom test was suggested [112]. In 19 eyes with probable angle-closure and normal IOP, a positive prone test occurred in 11 (56%). A positive darkroom test was found in 10 (53%) The combination of the two tests gave a positive result in 90%. Harris reported that patients with the greatest pressure rises consistently had gonioscopically visible angle-closure. In those with less pronounced pressure rises, the gonioscopic features were more variable.

When the pupil is dilated, obstruction of the trabecular meshwork as a result of thickening of the peripheral iris was believed to be the mechanism for IOP rises in the mydriatic test. In addition, if sympathomimetic agents are used, the posterior force vector from the dilator muscle increases and in theory substantially increases the pupil-blocking force. When cycloplegic agents are used, the tone of sphincter muscle is reduced and the anterior chamber depth is slightly increased as a consequence of changes in the ciliary muscle. In this case, the pupil block component is reduced rather than enhanced. Therefore, sympathomimetic agents, such as phenylephrine, are a more logical choice for provocative test. Because of the potential risk of an acute attack, mydriatic provocative testing is seldom performed in clinical practice.

Mapstone reasoned that both pilocarpine and phenylephrine used

simultaneously would be the best method of inducing pupil block [113]. The basis for this provocative test is that the agents stimulate the contraction of both sphincter and dilator muscles. The resultant posterior vector from the action of both muscles will increase the "pupil-blocking" force. In 109 eyes (100 patients) with intermittent symptom or fellows eyes of those suffering unilateral acute or chronic angle-closure, the pilocarpine-phenylephrine provocative test resulted in a positive result in 62% within 2 hours. The tropicamide test used in the same group of patients did not induce any positive results.

Pavlin suggested using darkroom UBM imaging to examine subjects, avoiding illumination necessary during gonioscopy (which will influence the configuration of the angle), to investigate the drainage angle configuration after exposure to stimuli intended to induce angle-closure. , Pavlin's group claimed UBM provocative testing has higher sensitivity in identifying high risk eyes.[114]

All of these provocative tests have been used in assessment of cases presenting with narrow angles and normal IOP, with the aim of identifying individuals at highest risk of developing appositional closure and a consequent rise in IOP. The ultimate aim is to rationalize the decision of which patients to treat. However, none of these tests have gained universal recognition as having sufficiently high predictive power to be used unquestioningly. The issue of variation in efficacy of these tests in different populations has not been thoroughly explored. Although the evidence is limited from the nature history of PAC and PACG development, Lowe and Wilensky have both asserted that provocative tests are probably poor predictor of future natural history.[105;115] This remains opinion rather than evidence. However, given the time and effort required to perform the tests and their perceived limited benefit, most practitioners in the West have given up using them in the clinical routine.

1.8 Racial differences in the angle-closure mechanism

Some studies suggested non-pupil block mechanisms play a more prominent role in angle-closure in East Asian eyes, relative to that seen in Europeans. Hung PT found positive dark room prone provocative test (DRPT) in 60% of Chinese eyes with early angle-closure (less than 4 clock hours of PAS) after

iridectomy, compared with 12.5% of "normal" eyes having a positive test result.[116] In a report of a series of cases from a Chinese hospital, where 35 eyes with symptomatic PAC and 37 eyes with asymptomatic PAC were examined, Wang et al found a positive DRPT in 11% of symptomatic and 32% of asymptomatic PAC after surgical iridectomy.[100] A retrospective study in Singapore found laser PI alone was insufficient to control IOP in over 90% of eyes with PACG (with established glaucomatous optic neuropathy)- a much lower success rate than in European eyes. It was suggested that this indicated a greater contribution of non-pupil block, and a greater susceptibility toward the development of chronic angle-closure in Asian eyes. The validity of this evidence may be affected by the fact that patients selected in Singapore tended to have late-stage disease with significant PAS and glaucomatous optic neuropathy. This was later evident in another study in which the success rates of laser PI were similar in 51 patients (80 eyes) in a clinic in New York and 65 patients (83 eyes) in Singapore with established PACG (i.e. with glaucomatous disc and field damage).[117] The rates of eyes requiring further additional treatment after laser PI were 100% in New York eyes and 94% in Singapore eyes (laser PI was assumed still to be the standard initial treatment for all chronic cases).

If East Asian eyes are more prone to non-pupil block angle-closure, the relative proportion of cases in a population setting remains uncertain. This is an important deficiency in our understanding from the perspective of public health policy because laser PI might be a simple preventive strategy for eyes with pupil-block. However, simple, effective intervention strategies for non-pupil block angle-closure are not yet recognised. If non-pupil-block PAC accounts for the majority of cases in East Asian populations, community-based intervention would be very difficult and challenging.

1.9 Management of primary angle-closure

Management of primary angle-closure glaucoma differs considerably from that used in open angle cases because of the fundamentally different mechanisms of the two diseases. Concepts of natural history and disease staging of PACG start with anatomical abnormalities of the anterior segment (narrowing of the drainage angle), followed by structural and functional damage of the anterior segment

manifested by PAS, an intermittent then sustained rise in IOP, and subsequently glaucomatous optic neuropathy(GON). This "end organ damage" is the final pathway for all forms of glaucoma.

Management of the early stages of PAC(G) focuses on the modification of the anterior configuration, hopefully before irreversible trabecular damage and GON develops. When GON has developed, the aim of the treatment is to lower the IOP in order to prevent the progression.

Laser, surgery and medical treatment are all recognised options for modifying the anterior drainage angle configuration. Peripheral iridotomy (laser PI) and iridoplasty are two laser treatments for opening a narrow angle. Surgical iridectomy or lens extraction are surgical procedures that have been used for a similar purpose. Pilocarpine is effective in opening the drainage angle in many cases.

1.9.1 Surgical and laser peripheral iridotomy

Laser iridotomy remains the cornerstone of management of angle-closure. It results in a significant increase in angle width in both Europeans and Asians with narrow angles.[118;119] One study of predominantly Chinese people with narrow drainage angles found PI produced a significant increase in angle width. It was also noted that the changes in iris profile following PI varied according to illumination level, when PAC suspects and age-matched normal controls were compared. It was suggested that an additional, unidentified mechanism was responsible for angle occlusion in the dark, independent of pupil-block.[118] The efficacy of PI for disease control is dependent both on the underlying mechanism causing closure, and the stage of the disease. Among people of African and Asian descent, greater extent of PAS, a higher presenting IOP and a larger cup:disc ratio are all predictors of poor pressure control following iridotomy.[120;121] Following an episode of symptomatic angle-closure, reports suggest satisfactory IOP control can be achieved in 42 to 72% of cases with PI alone.[122;123] Once GON (defined as structural damage to the disc and a field defect), has developed, virtually all cases (94 to 100%) will require further treatment to control IOP.[117] Confirmation of the inference that earlier intervention will definitely

lead to a superior outcome in the long-term is hindered by the phenomenon of "lead-time bias"- the concept that earlier detection and treatment merely increase the period of follow-up, until the time when control of disease is lost, with no change in outcome for the individual. However, the efficacy of prophylactic iridotomy or iridectomy in the fellow eye of one that has suffered "acute" angle-closure, in both Europeans and Asians (89 to 100% control of IOP),[122;124] is a persuasive argument that iridotomy, performed at an early stage in the disease process, does indeed have a beneficial effect.

PI eradicates relative pupil block and equalizes the pressures in the posterior and anterior chambers. In a small series of eyes with PAC (12 eyes of 6 patients, racial origin not described), examined using Scheimpflug photography before and after iridotomy, Jin and Anderson found the iris profile changed after iridotomy: the pupillary zone of lens-iris contact increased, and mid-peripheral iris convexity disappeared and, the steep iris profile in the extreme periphery flattened[125].

In the West, anterior rotation of the ciliary body, supporting and preventing posterior movement of peripheral iris (typical plateau iris configuration) is widely believed to be the main cause of the angle failing to widen after iridotomy. However, the anatomical features in cases of persistent post-iridotomy angle-closure may be more complex than we previously suspected. In a group of patients who had undergone iridotomy, Garudadri found that an anteriorly-located ciliary body was identifiable by UBM in 41% of eyes in which angle width had increased following iridotomy.[126] This observation suggests that even in eyes affected predominantly by pupil block (where angle width increased following PI) anterior rotation of the ciliary body is evident.

1.9.2 Laser peripheral iridoplasty

Argon laser peripheral iridoplasty (ALPI) is another measure that can increase drainage angle width by applying contraction burns (low power, large spot size, long duration) to the peripheral iris, creating a space between the anterior iris surface and the trabecular meshwork. This treatment was first described by Kimbrough et al in 1979,[127] in nanophthalmos and later on by Weiss in patients

in whom angle width did not increase following iridectomy.[128] Weiss et al reported that 17 of 20 eyes (85%) had IOP controlled (<19 mmHg) with a median follow up period of 18 months.[128] They also stated that the unsuccessful cases were mainly in those with longer duration of angle closure (90 days), suggesting a broad PAS may compromise the efficacy of this treatment. Ritch reported results with a much longer period of follow-up (mean 79±8 months (range, 72-188 months.[129] In 20 of 23 (87%) eyes, the angle remained open throughout the entire follow-up period after one treatment. Only 3 eyes closed between 5 to 9 years, and required a repeat treatment to achieve re-opening.

ALPI was also used as an initial treatment for acute PAC in order to open the drainage angle prior to laser iridotomy to eradicate pupil block. Lam et al reported using immediate ALPI in 10 acute PAC patients in Hong Kong. The IOP dropped from a mean of 59 mmHg to 16 mmHg in 60 minutes. In nine patients with corneal oedema, this cleared within 1 hour. No complications were reported.[130] A randomized controlled trial was then conducted. IOP was found to be significantly lower in the iridoplasty group, compared with those treated by medication, at 1 hour (32 cases in ALPI and 40 cases in medication arm). The difference between the two groups was no longer significant after 2 hours.[131] Again, no post-laser complications occurred in this group of patients. A longer follow up (mean:33 months, range: 16-48 months) was subsequently conducted for eyes treated with immediate ALPI followed by laser PI.,[132] Among 33 eyes of 32 patients, 21 (70%) had normal IOP without medication, however, 9 eyes developed elevated IOP (> 21 mmHg). Three subjects died, or underwent cataract surgery or became loss to follow-up. Among these 9 eyes, 6 required only topical medication and 2 required phacoemulsification with goniosynechialysis to control IOP, one refused surgical intervention.

1.9.3 Trabeculectomy in angle closure

Since Cairns proposed a modified trabeculectomy technique in 1970s,[133] substantial further modifications have been made in order to reduce potential complications and achieve better IOP control. These refinements include the use of anti-scarring agents and adjustments to exact surgical technique. In angle-closure glaucoma, the application of trabeculectomy usually depends on

the clinical types and staging of the diseases.[134] In most of the cases presenting with acute episode, primary trabeculectomy is occasionally considered if the IOP is unresponsive to intensive medication and corneal edema precludes laser PI. In some cases suffering a symptomatic episode may subsequently develop chronic synechial angle-closure, which may also be treated by primary trabeculectomy.

In Singapore, a study of 32 eyes suffering acute PAC eyes in which medical treatment failed to control IOP (surgery performed in 1993-1995), trabeculectomy did result in satisfactory IOP control in over half of cases (56%) suggesting that trabeculectomy on inflamed eyes is associated with a proportionally lower success rate.[118;135] The author argued that this relatively low success rate was due to the inflamed eye and the IOP markedly increased and therefore suggested conventional trabeculectomy should be avoided in eyes with severe, medical irresponsive APAC, thus peripheral iridoplasty,[130;136] or paracentesis,[137;138] may appear to be better choices to break the acute attack when unresponsive to medication before the trabeculectomy surgery

In the same study in Singapore, in 24 eyes with medically controlled angle-closure but with extensive PAS (>180 degree) or glaucomatous disc damage (VCD >0.5), trabeculectomy achieved a very high success rate (87%) for pressure control, comparable to the others performed in POAG eyes. [139] However, because the study was conducted retrospectively, it is difficult to prove if the conventional laser or surgical iridectomy can achieve the same level of success in these cases.

There is no consensus on specific indications, target IOP and prognosis in using trabeculectomy in chronic PACG. Observational studies suggested that laser PI alone fails to control IOP particularly when GON is established (as described above).[122] Salmon reported that over one-third of all angle-closure glaucoma patients underwent trabeculectomy.[121] Sihota reported that in 70 eyes diagnosed with chronic PACG, elevated IOP, extensive PAS and established GON, medical therapy alone was able to achieve IOP control in 65%. Among them, most had mild glaucomatous field loss, although trabeculectomy was required in the rest of (35%), when medical therapy failed to control IOP in the 6-year follow-up

period.[140] Among these eyes treated by trabeculectomy, 25% eventually required additional medications. This failure rate was comparable to Wilson's report in 1977 where 80% of 112 chronic PACG patients had IOP < 21 mmHg at a 7-year follow-up.[139]

The increasing effectiveness of glaucoma medication, such as the emergence of prostaglandins drops, is challenging the usage of trabeculectomy as the first line choice of glaucoma, not to mention, the early and late complications of the surgery that include severe adverse events, such as malignant glaucoma or endophthalmitis.

1.9.4 Lens extraction

In the mechanism of angle-closure, Lowe and Mapstone described that pupil-block and appositional closure of the drainage angle is aggravated when the point of iris-lens contact is situated anterior to the iris root.[73;92;141]. Other mechanisms at the level of lens (phacomorphic glaucoma) and posterior to the lens (for example, malignant glaucoma) also emphasize the importance of the contribution of the lens in angle closure.[142] Therefore, removal of the lens may help alleviate the mechanisms responsible for angle-closure in these cases.

Greve first proposed extracapsular cataract extraction (ECCE) with posterior chamber IOL implantation alone to treat PACG[143]. In 21 eyes of 20 patients with PACG, ECCE/IOL lowered the IOP to normal in 16 eyes, only 5 eyes required additional medication after the procedure. Afterward, Gunning and Greve advocated "intercapsular" or extracapsular cataract extraction and IOL implantation to treat the various types of angle-closure glaucoma, even in eyes with relatively good visual acuity.[144] In 67 eyes of 57 patients, lens extraction achieved an IOP reduction in 55% of eyes suffering acute PAC, 44% of uncontrolled PACG eyes, while 94% of all eyes achieved an IOP < 21 mmHg in long term follow-up. The efficacy of ECCE in the treatment of PACG was further evident in reports from South Africa[145] and Taiwan.[146] Yang et al further documented a deepening of the anterior chamber and widening of drainage angle after IOL implantation using Scheimpflug imaging.[146;147] A study in the UK

compared the IOP lowering effect of ECCE in PACG and POAG eyes (as controls). The results indicated the significant IOP lowering effect in PACG groups – with over 65% of PACG eyes achieving IOP < 21 mmHg in the long term-- but the IOP level in POAG were primarily unaffected.[148] This comparison with POAG may shed light on the aetiology of the IOP lowering effect.

Phacoemulsification (phaco/IOL) uses a small incision and foldable intraocular lens, typically eliminating the need for sutures, and shortening surgical time. In a uncontrolled cases serials, Ge J et al demonstrated the success of phacoemulsification in lowering IOP and deepening of central anterior chamber (changes on limbal ACD was not described) in 47 PACG eyes (26 acute, 12 chronic, 2 secondary eyes) in Chinese eyes.[149] Jacobi et al studied the efficacy of phaco/IOL by comparing to the conventional surgical iridectomy in 43 eyes of 43 patients with acute PAC.[150]. Primary phaco/IOL did better in terms of IOP reduction, anti-glaucoma medication, best-corrected visual acuity and the need for additional surgical intervention. The complication of fibrinoid aqueous reaction was found to be less in primary phaco group.

However, lens extraction alone is not able to achieve satisfactory IOP controls in all PACG eyes. The success will probably depend on the extent, duration and intensity of the angle-closure. Those with long-standing peripheral anterior synechiae will probably have a poor prognosis. In order to cope with the extensive PAS formation, goniosynechialysis (GSL), a surgical procedure that breaks the adhesions between trabecular meshwork and peripheral iris, has been popular in Japan although it is not overwhelmingly accepted in the other countries because of the potential side effects and uncertain efficacy.[151-153] In a prospective, uncontrolled study explored the efficacy of phaco/IOL plus GSL in 52 eyes of 48 patients suffering acute PAC and uncontrolled IOP after laser PI, Teekhasaenee and Ritch reported IOP was controlled without medication in 90% of eyes, and only 1 required filtration surgery, the study also documented extent of PAS was reduced. PAS and elevated IOP did not recur between 3 months and 6 years, suggesting the progression of PAS perhaps was stopped when the lens was removed.[154] However, because the study did not have a control group, it was not able to prove the advantage and necessity of GSL in these acute cases. Furthermore, the success of GSL also depends on the absence of functional

damage to the trabecular meshwork that probably occurs with long-standing PAS.[155] This argument may be more relevant in chronic PAC when extensive PAS formation and non-pupil block mechanisms underlining the angle-closure, and the duration of PAS formation may be much longer. In a small case serials (7 eyes), Lai and his colleagues reported an absolute success rate of 100% for IOP control (< 21 mmHg without medication) and visual acuity improvement after a combined surgery of phaco/IOL and limited GSL followed by diode laser peripheral iridoplasty. [156] Again, this study lacked a control group, and hence the study was not able to demonstrate the efficacy of GSL and diode ALPI in chronic PAC over no treatment.

2. Definitions, Subjects and Methods

2.1 Definitions

The definitional criteria developed by ISGEO were used in the current field study.[9] Because definitive information on the presence of glaucomatous disc and field damage is not always available in field studies, the identification of glaucoma can be made on 3 levels of evidence. The highest level of evidence requires optic disc and visual field evidences (VCDR or asymmetry > 97.5th percentile and reproducible glaucomatous field defect). In the second, if the visual field test could not be performed satisfactorily, a severely damaged disc (VCDR or asymmetry > 99.5th percentile) is considered compatible with glaucoma. The 3rd level of evidence specifies that if the optic discs cannot be examined due to severe media opacity, subjects who are blind (corrected visual acuity < 3/60) and have undergone previous glaucoma surgery, or have an IOP greater than 99.5th percentile are classified as suffering glaucoma. The division of cases of glaucoma into PACG and POAG was based on the gonioscopic finding of an occludable angle (where the posterior, usually pigmented, trabecular meshwork is not visible for 270 degrees or more during a static examination) or a reliable medical history, if the angle status has been changed by previous treatment. Elevated IOP and PAS formation were not considered prerequisites for the diagnosis of PACG. If an eye with occludable drainage angle and feature indicating that trabecular meshwork obstruction by peripheral iris and with normal optic disc and visual field, this was called primary angle closure (PAC); if an eye only presented as occludable angle without any evidence of trabecular meshwork obstruction, this was called primary angle closure suspects (PACS).

2.2. Sampling and Enumeration

Ethical approval was obtained from the Zhongshan University Ethical Review Board and Ethical Committee of Zhongshan Ophthalmic Center. The study was conducted in accordance with the Tenets of the World Medical Association's declaration of Helsinki. Examination of the subjects for the cross-sectional survey was carried out in September 2003 to February 2004. Laser iridotomy

was conducted in January 2004 to March 2004.

The study subjects were enrolled from Liwan District, Guangzhou. Liwan district was one of ten administrative districts in Guangzhou. In the history of Guangzhou urban development, Liwan is one of the oldest districts (**Figure 10**). The socio-economic status of most residents is upper-middle class. The population in 2000 Census was 514,600. The life expectancy in Guangzhou was 77.21 years in average, 74.73 years in men and 79.90 yeear for women. These figures were higher than average level in the whole country: 72.40 years in average, 69.93 for men and 73.33 for women. The decision to select this district as the survey site was made because of its stable, older population. One Street Block, Fengyuan Street, with a population 62,815 occupying 0.77 square kilometers was arbitrarily selected because it was mainly a residential area with a limited number of commercial and industrial buildings. Cluster sampling was used to select the study sample in this street block. The clusters were defined geographically by the boundaries of the Residence Administrative Committees (RACs) subdivisions. There were 10 RAC "clusters" with approximately equal populations (6,000). These 10 geographically-defined RAC areas were used to randomly choose 2 specific clusters.

The individuals aged 50 years and over who had been living in the target site for more than 6 months were considered eligible during the enumeration. Using the Household Resident Register record kept by the district government, households with eligible subjects were identified by the address, name of household head, name of subjects and date of birth. A total of 2,313 eligible subjects were identified from the Register. These households were then individually visited by enumerators from local RAC units, supervised by district government officials and delegates from the research team. Making up to three visits, the enumerators verified if the enumerated subjects were still resident at the address. Once contacted, invitations or appointments were distributed, and written informed consent was obtained, after explaining the purpose of the study and the risks and benefits of the examination. Detailed personal information (age, gender, date of birth, address, phone contact information) was also collected. Subjects who did not attend the examination were then contacted by phone by local RAC staff and study investigators, to further encourage the

attendance. For those who expressed reluctant on the phone, further visits were made by local community volunteers and the individuals who had completed the examination and benefited from the diagnosis and treatment. For those who decided to refuse the examination, a simple questionnaire recording the visual function, previous glaucoma, ophthalmic history and reasons for refusal was administered by phone.

Figure 10 Landscape of the Liwan District, Guangzhou

2.3 Examination in the cross-sectional survey

The community examination site was set up in a 2-storey house. This was located at the center of the Fengyuan Street Block, and within half an hour's walk for most of the subjects. Examinations were scheduled between 9am and 5pm from Monday to Friday. Examinations over weekends were introduced in the 2nd month of examinations in order to facilitate the participation of the younger subjects who worked on weekdays. Approximately 50 subjects were scheduled for the examination per day. The field examination procedure was as follows.

2.3.1 Registration, questionnaire and weight / height measurements

Identity of the subjects was verified by subjects' official identity cards or retirees cards with photos. A questionnaire was administered by an interviewer in order to collect details of ophthalmic history, general medical history, income and education. Weight and height were then measured without coat and shoes. The questionnaire, interviews and weight/height measurement were not available during the 1st week of the examination.

2.3.2 Visual acuity testing and refraction

A nurse used a handheld autorefractor (ARK-30, Nidek Corp.) to measure the non-cycloplegic refraction. The autorefractor produced eight refraction values, each with a machine-calculated confidence index, along with an average weighted value. If the autorefractor could not generate any valid readings, the examiner recorded a failure. Clinical information on reasons why autorefraction failed were not recorded because they were difficult to judge at this stage of examination.

Distance visual acuity was measured by a nurse using an ETDRS logMAR E chart (Precision Vision, Villa Park, Illinois, USA) with standard illumination box. Visual acuity measurement began at a distance of 4 meters with the top line (6/60). If the orientation of at least four of the five optotypes was correctly identified, the subject was then tested by dropping down to line 4 (6/30). If one or less optotypes is missed, the testing continued at line 7(6/15), continuing to line 10 (6/8) and finally line 11 (6/6). If any level the subject failed to recognize four of the five optotypes, the line immediately above the failed line was tested, until successful. If the top line at 4 meters is failed, the subject was advanced to 2 meters and then 1 meter with progression down the chart as described above. The lowest line read successfully was assigned as the vision for the eye. For those with visual acuity worse than 3/60, such as finger counting, hand motion, no light perception, the visual acuity was recorded as such with the examination distance. The presenting vision with daily-use correction was recorded first (refractive correction was recorded as well), and then the best-corrected vision

using the autorefraction result after necessary refinement in order to achieve best-corrected visual acuity for those with presenting visual acuity < 6/12 in either eye.

2.3.3 Intraocular pressure and slit lamp examination

IOP was estimated by using a Tono-pen (Mentor, MA, USA) device by a nurse after instilling topical anesthesia (0.4% Oxybuprocaine, Santen, Japan). Internal calibration program was run before use every day. The measurement was repeated if the SE of the measurement was > 5%. One measurement was taken and recorded for each eye.

Slit lamp examination (Topcon SL-8Z with Nikon-D1x digital image system) was then carried out to record evidence of any abnormalities of the anterior segment by primary investigator (M He), including evidence of ischaemic sequelae of PAC, secondary glaucoma and lens opacity. Gonioscopy was then carried out using a Goldmann-style one-mirror lens (Model 902, Haag Streit, Bern, Switzerland) at a x25 magnification with low ambient illumination. A narrow vertical beam 1 mm in length was offset horizontally for superior and inferior quadrants, vertically for nasal and temporal quadrants. Care was taken to avoid light falling on the pupil. Small movement of the lens was allowed to visualize the drainage angle but large movements were avoided because of the possibility of indentation. Dynamic examination with Goldmann lens was carried out after static gonioscopy of 4 quadrants was completed (alternatively, a four mirror Zeiss lens was used if the visualization by Goldmann lens was not satisfactory). Spaeth grading system was used for the recording the results (See Introduction section). Geometric angule width in degrees was recorded for superior and inferior quadrants only, as similar estimation in nasal and temporal quadrants was found to be difficult. Apparent iris insertions (depending on the visibility of anatomical landmarks of the drainage angle by static gonioscopy) and "true" iris insertion (based on visibility of anatomical landmarks of the drainage angle during dynamic gonioscopy) were recorded for 4 quadrants. Iris profile was recorded as either regular, steep, concave or plateau. Any PAS found was recorded in details, including the circumferential extent and height of PAS, by drawing on a gonio-gram. Slit lamp photography system was used to record any significant

abnormalities with patients ID when necessary. Because the gonioscopy was carried out before the axial anterior chamber depth (AACD) measurement, the examiner was unaware of the AACD results during gonioscopy.

The examiner then classified the subjects into angle-closure suspects and normal control groups, after exclusion of those with established angle-closure. By using the result of apparent iris insertion, the examiner identified the subjects as angle-closure suspects when the pigmented TM was not visible in 2 or more quadrants. Normal control subjects were selected systematically, 1 of 10, in those identified as not meeting the criteria of angle-closure suspects. All subjects with aphakia, pseudophakia, pterygium or corneal opacity were excluded.

2.3.4 Optical pachymetry

Optical pachymetry (Device I and II, Haag-Streit, Bern, Switzerland) mounted on slit lamp (Model 900, Haag-Streit, Bern, Switzerland) was used to measure the central anterior chamber depth (ACD) and central corneal thickness (CCT) by another ophthalmologist for all the subjects. The "touch" method of measurement was used throughout. The subject was instructed to gaze in the primary position. The brightest, narrowest illumination beam was used. The measurement of ACD and CCT were made using the pupil margin as the reference for the centration. CCT was measured using Device I at x1.6 objective magnification with +2.5D eyepiece addition, read to the nearest 0.01 mm. ACD (anterior corneal epithelial surface to the anterior lens capsule), was measured to the nearest 0.05mm using Device II at x1 objective magnification and +6D eyepiece addition. Three measurements were carried out and the median of the 3 readings was recorded. "True" ACD from endothelial surface of the cornea to the anterior lens capsule was calculated by subtracting the corneal thickness from the ACD reading values. No correction was made for the corneal curvature.

2.3.5 Examination of angle-closure suspects and normal controls

The subjects enrolled as angle-closure suspects and normal controls were re-examined by another ophthalmologist, using a separate examination form. This examiner was masked to the findings on gonioscopy and classification. The

traditional oblique flashlight test was carried out initially and recorded as being of 3 separate categories: deep, medium and narrow. The penlight was directed from the temporal side of the eye so that oblique penlight illumination across the surface of the iris. If both temporal and nasal sides of the pupil were fully illuminated, it was classified as "deep"; if only part of nasal iris was illuminated, it was classified as "medium"; if only the temporal iris was illuminated, it was classified as "narrow". After this "standard" penlight oblique test, a modified slit lamp simulated oblique flashlight test was then carried out to exactly measure the length of the iris shadow and the diameter of the cornea (**Figure 11**). The examination was carried out by slit lamp (MODEL 900 BQ, Haag-Streit, Bern, Switzerland). The patients were asked to gaze straight forward in primary position, a wide bright beam was offset from the temporal side at an angle of 90 degree to the axis of the direction of gaze, so that the offset beam was parallel to the iris plane. The reticule eyepiece (Haag-Streit, Bern, Switzerland) was used to measure the length of iris shadow (A-B in the **figure 11**) and corneal diameter at the horizontal direction crossing the center of the pupil at x10 magnification. The limbus was defined as the margin of the cornea. Those with pterygium reaching the limbus were excluded in this evaluation.

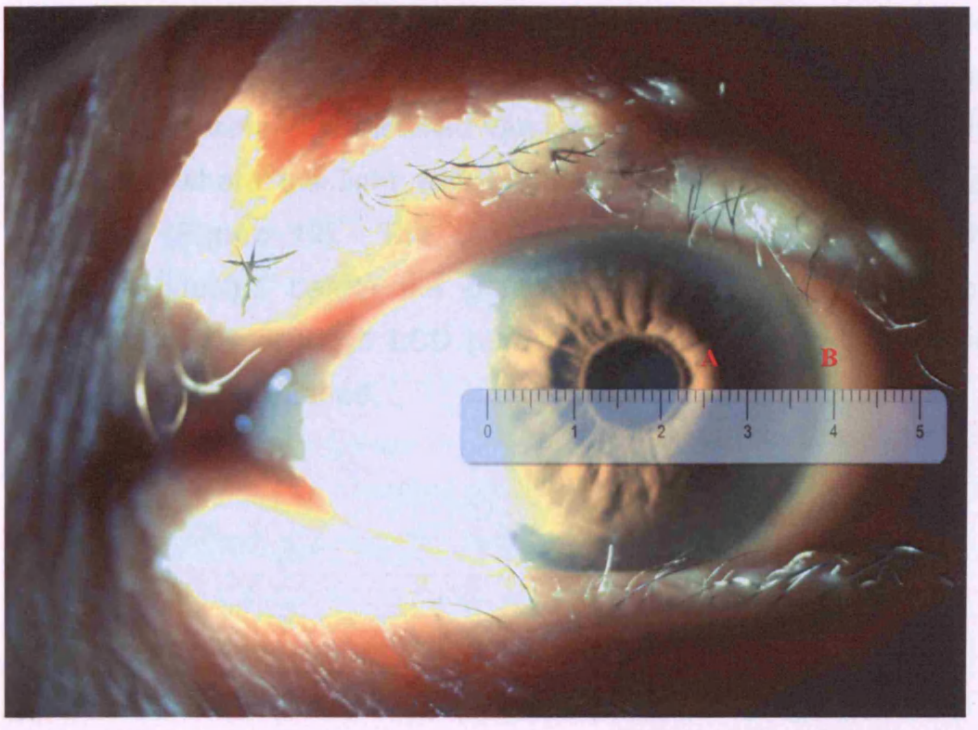


Figure 11 Landmark for the reticule measurement of oblique flashlight test. A: margin of the iris shadow, B: margin of the corneal limbus. The measurement was a simulation.

The standard van-Herick test was performed first. The van-Herick test was then conducted again using standard photos (See Introduction section) followed by reticule van-Herick test. This examination was carried out using a slit lamp (Model 900 BQ, Haag-Streit, Bern, Switzerland). The illumination column was offset at an angle of 60° to the axis of the microscope. The brightest, narrowest possible vertical beam of light was projected at the temporal limbus so that the beam of light fell perpendicularly onto the ocular surface. The beam was positioned on the most peripheral part of the temporal of the cornea that would allow a clear view of the anterior chamber and peripheral iris simultaneously. In the eyes with significant irregularities on the iris surface, such as iris rolls, crypts, the location for LCD measurement was defined as the narrowest point as long as there was not a spike on the iris surface at this location. The objective magnification was x 16 overall. The LCD was graded in 7 categories with reference to standard photos described by Foster et al.[46] An eyepiece measuring graticule (Haag-Streit, Bern, Switzerland) was then used to measure the distance from epithelial surface to endothelial surface of the cornea (corneal thickness) and the distance from the iris to the endothelial surface of the cornea (limbal anterior chamber depth) after re-adjusting the magnification to x 25 overall (**Figure 12**). The offset angle and location of this measurement were identical to those on the modified van-Herick method. The band on the iris was defined as where the light was brightest if the light offset on the iris was dispersing (**Figure 12**). The LCD measurement with standard photos was always conducted before the graticule measurement method so that the examiner could not judge LCD percentage in standard photos based on the results in graticule method.

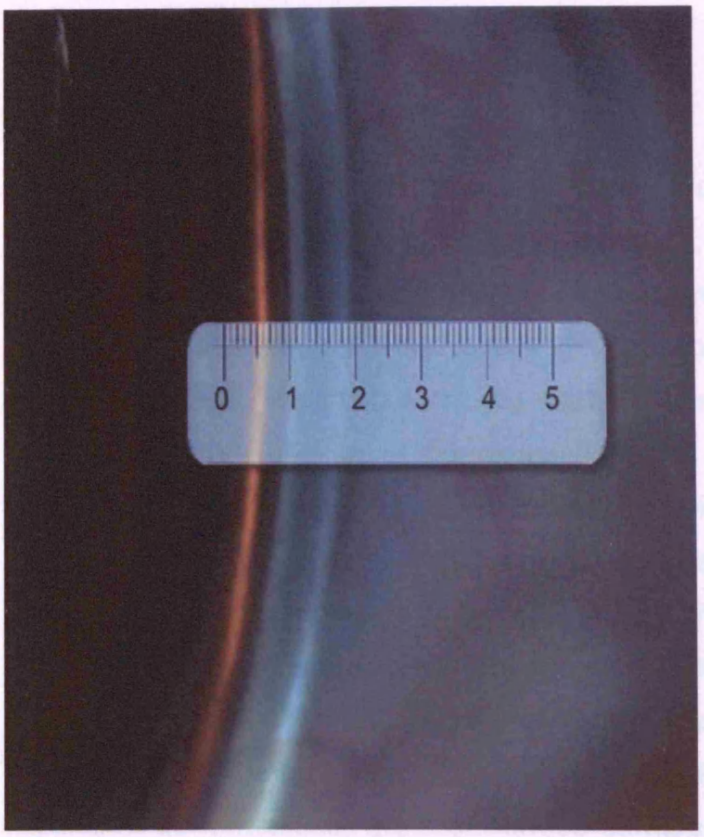


Figure 12 Simulation of graticule method of measuring limbal chamber depth

2.3.6 Ultrasound biometry

Anterior chamber depth, lens thickness, vitreous length and axial length of the globe were measured by A-mode ultrasound (Echoscan US1800, Nidek, Corp., Japan) before pupil dilation by a nurse. The patients were in sitting position. A handheld probe (applanation) was used for the measurement. The best trace figure of 10 individual measurements for each parameter was taken. If the standard deviation was more than 0.13mm for the ACD value, the readings with largest variation were deleted and the measurement repeated. The ACD reading obtained from this measurement included the corneal thickness according to the operation manual. Ultrasound pachymetry was carried out using the same machine and pachymetry probe at the center of the pupil, 10 individual measurements were automatically taken and afterward the average of 10 values was recorded.

2.3.7 Optic disc examination

The optic disc was examined using a slit lamp (Model 900 BM, Haag-Streit, Bern, Switzerland) and +78D lens at x 16 magnification, initially without pupil dilation. The vertical CDR was measured as the key outcome measure. Measurement of vertical disc diameter excluded areas of parapapillary atrophy and Elschnig's ring (scleral ring). The margins of cup were defined by stereoscopic view as the point of maximum inflexion of the vessels crossing the disc rim. Standard photos for the VCDR from 0.1 to 1.0 at 0.1 increment units were used for the grading, and the measuring graticule was not used. Disc hemorrhage and notching were recorded. If the stereo view was not satisfactory, the pupil was dilated using 1% tropicamide plus 2.5% phenylephrine,provided that the drainage angles were not classified as occludable. If the view of the optic disc was still not satisfactory, "disc not seen" was recorded. For all eyes with VCDR 0.7 or above, or with other significant abnormalities, a stereo-fundus camera (Model 3-Dx, Nidek, Japan) was used to obtain disc photographs for both eyes.

2.3.8 Visual field

Those people with suspected glaucomatous disc damage (VCDR $\geq$ 0.7 in either eye, VCDR asymmetry $\geq$ 0.2 or IOP $\geq$ 21 mmHg) were asked to return for visual field testing on another day. The VF test was not conducted on the same day because of the retinal bleaching that may have occurred during the rest of the examination. White on white static automated perimetry (Model 750, Zeiss Humphrey Instruments, San Leandro, CA, USA) was carried out using near refractive correction. The SITA-Fast 24-2 mode was used throughout followed by a SITA-standard if the first test was abnormal. If the reliability of the field test was not satisfactory (false positive > 33% or fixation loss > 20%) or there was a defect compatible with glaucoma or any glaucoma suspects with elevated IOP, the patients were called back for repeated field test on another day. A glaucomatous visual field defect was defined as a cluster of four or more contiguous points on the pattern deviation plot (P<5% occurring in age-matched normal subjects) not crossing the horizontal meridian. It was required that this defect was consistent with the location of the disc rim damage. A frequency

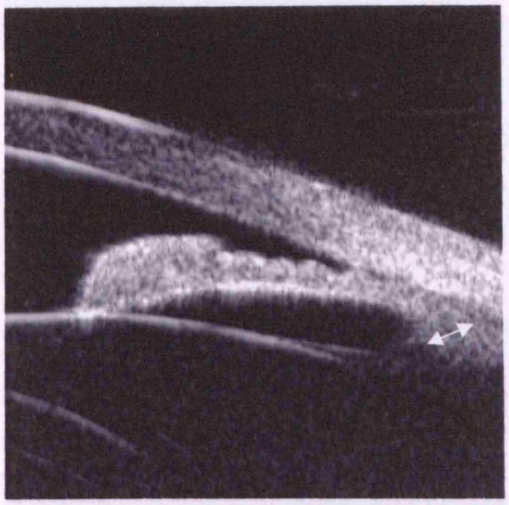
doubling test was performed as screening for some of the subjects at the beginning of the study but this was abandoned when the results showed a substantial false positive rate. All the patients eligible for field testing but who refused or could not attend were offered assistance and encouragement. The reasons for the not attendance was recorded.

2.3.9 Ultrasound biomicroscopy

All subjects identified as angle-closure suspects and normal controls were invited for UBM examination (P45 ultrasound workstation, Paradigm Med Ind. Salt Lake City, Utah, USA). UBM examination was conducted in the Zhongshan Ophthalmic Centre (ZOC) main hospital by a technician who had 8 years experience of UBM examinations. Free transportation was provided for the subjects. The technician was masked to the gonioscopic findings. UBM examination was carried out in a dark room with illumination below 5 Lux illuminations. Images of 4 quadrants and 1 image of the central anterior chamber were acquired in supine position. The subjects were asked to fixate on a ceiling target using the contra-lateral eye. Five target markers (fluorescent papers 5x5cm in size) were set up on the ceiling to guide the patients for the measurement on superior, inferior, nasal and lateral quadrants so that the angle between the gaze and the measurement axial was standardized to 20 degree, and accommodation could be controlled. Saline was used as coupling agent and topical anesthesia was used before the examination. The probe was always perpendicular to the ocular surface. The gain was set to between 60 to 80 db in order to have a clear display on the structure and minimize the ultrasound noise simultaneously. The criteria for acceptable images included: clear visualisation of the scleral spur, angle, ciliary body and a half chord of the iris. The tangent line of the anterior surface of the lens should ideally be horizontal ideally in order to ensure the layouts of the images were standardized. Repeated UBM image acquisition was carried out for 20 narrow angle eyes and 20 normal angle eyes as a quality control process.

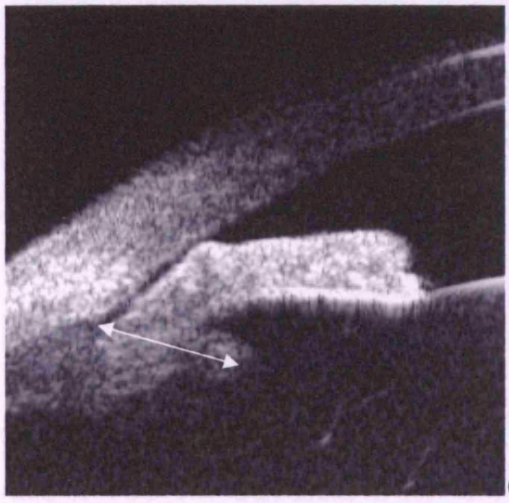
UBM Pro 2000 software (Paradigm Med Ind. Salt Lake City, Utah, USA) and a newly designed software program used for the image analysis. Reproducibility of the UBM image analysis was examined.

Quantitative parameters alone may not fully describe the features that we believe are associated with-angle closure, particularly the existence of appositional closure and anterior rotation of the ciliary processes. In order to describe the characteristics of the anatomical structures related to angle-closure, typical UBM images were selected to classify ciliary process size and rotation, level of iris insertion, iris convexity, iris thickness at basal (insertion), the presence of appositional closure (iris-TM contact) and the identification of a sinus between the peripheral iris and TM behind an area of irido-corneal contact. Examples are shown in **Figure 13-20** and described in the "Methods" section.



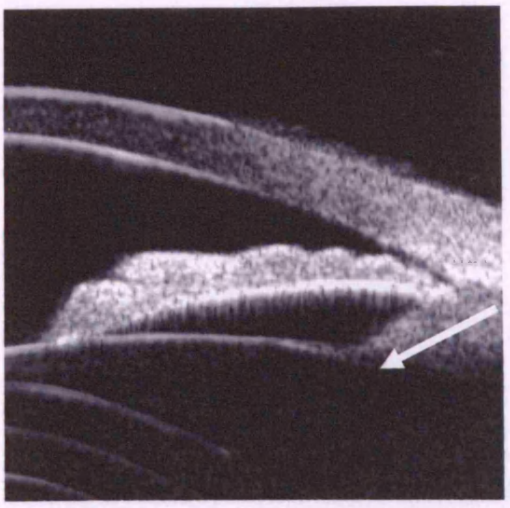
Ciliary body size: Small

Ciliary body size: Medium

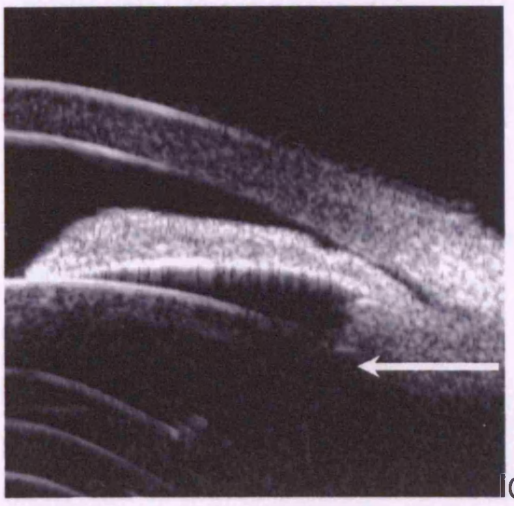


Ciliary body size: Large

Figure 13 Size of the ciliary body is estimated by its length relative to the limbal corneal thickness. a: Small: shorter than limbal corneal thickness (LCT); b: Medium: about equal to LCT; c: Large: one and half to two times as long as LCT.



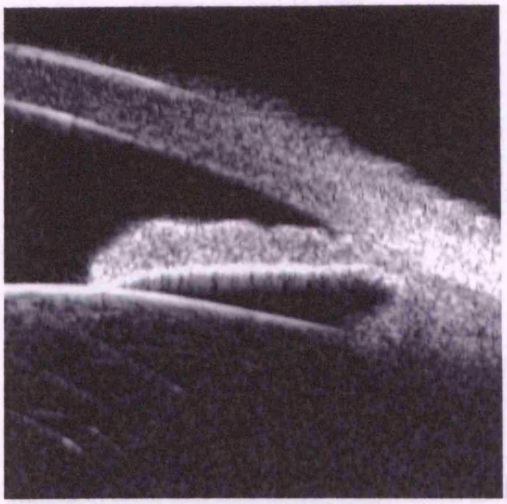
Ciliary body: Neutral



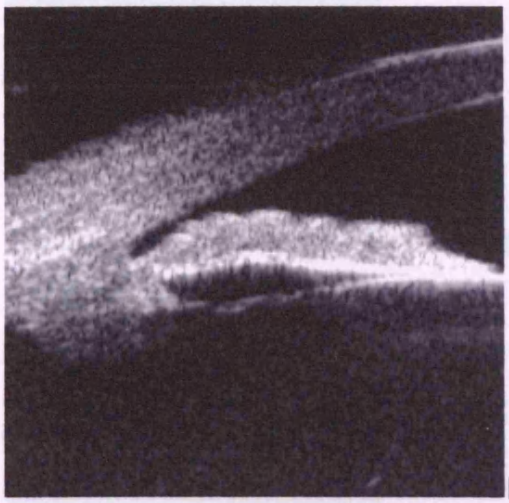
Ciliary body: Rotated

Figure 14 Direction of ciliary body

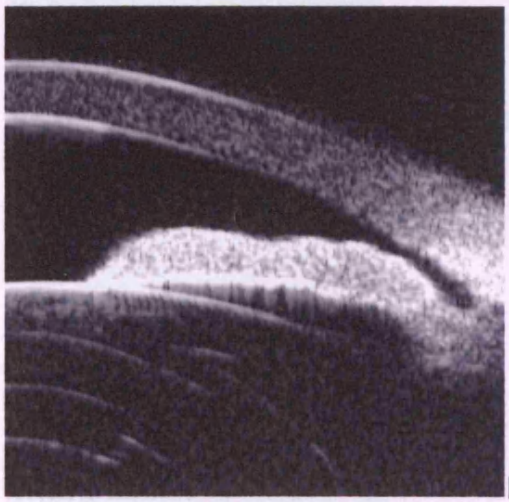
a. Neutral: the direction of ciliary body is at 45 degrees to the iris plane.
b. Rotated: this direction is parallel to the iris plane (Arrows show the direction of the ciliary body and processes).



Iris insertion: Basal



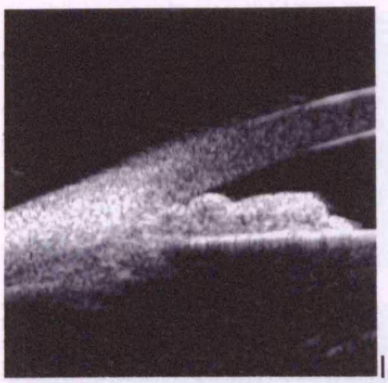
Iris insertion: Middle



Iris insertion: Apical

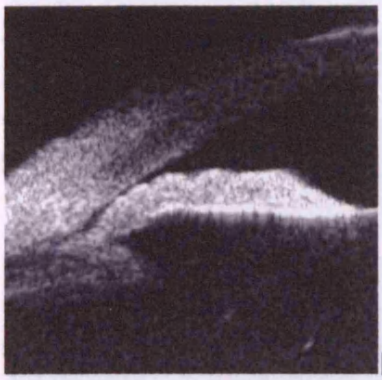
Figure 15 Location of the iris insertion:

a. Basal: insertion is near to the base of the ciliary body.
b. Middle: iris inserts into the middle of the anterior face of the ciliary body
c. Apical: iris insertion at the apex of the ciliary body.



Iris convexity: Absent

Iris convexity: Mild



Iris convexity: Moderate

Iris convexity: Extreme

Figure 16. Iris convexity is determined by the maximal displacement of the posterior surface of the iris relative to a line between iris root and pupil margin.

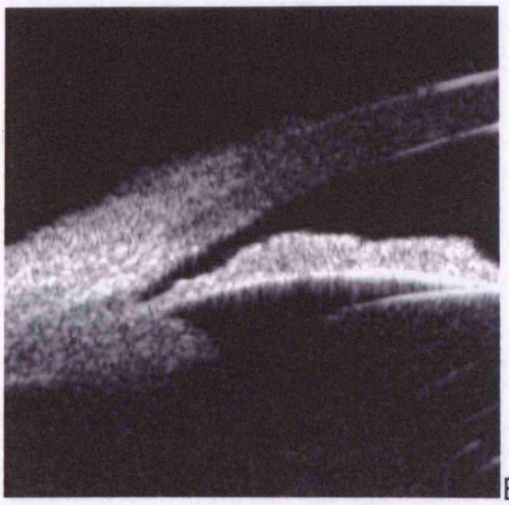
Overall iris thickness: Thin

Overall iris thickness: Medium

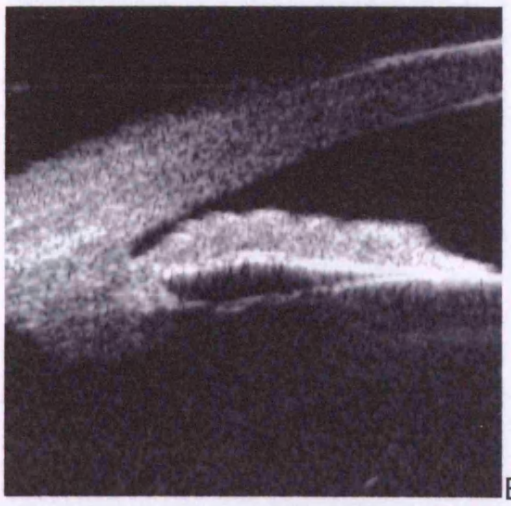
Overall iris thickness: Thick

Figure 17 The iris thickness in the whole length is classified relative to limbal corneal thickness (LCT)

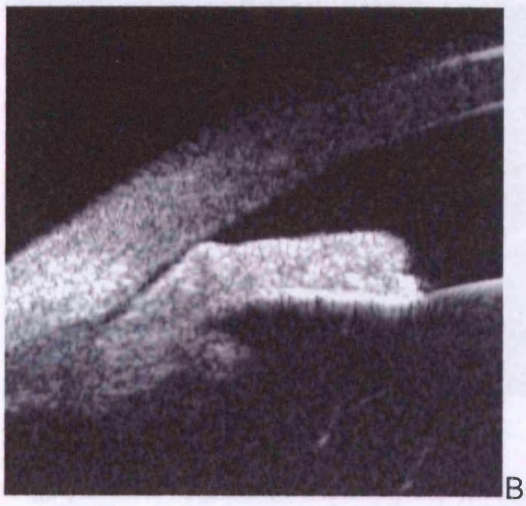
a. thin: less than 1 LCT.
b. Medium: near 1 LCT
c. Large: thicker than 1 LCT.



Basal iris thickness: Thin

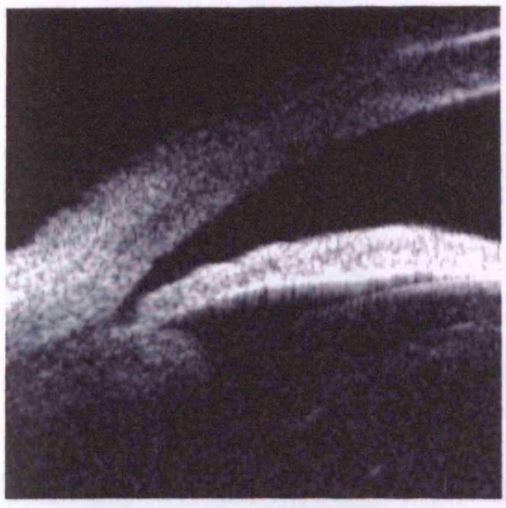


Basal iris thickness: Medium

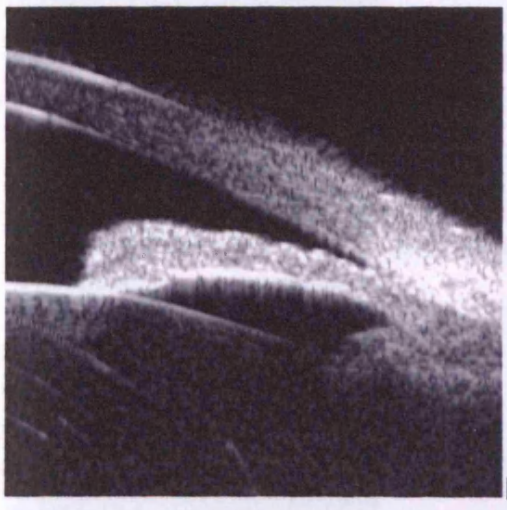


Basal iris thickness: Thick

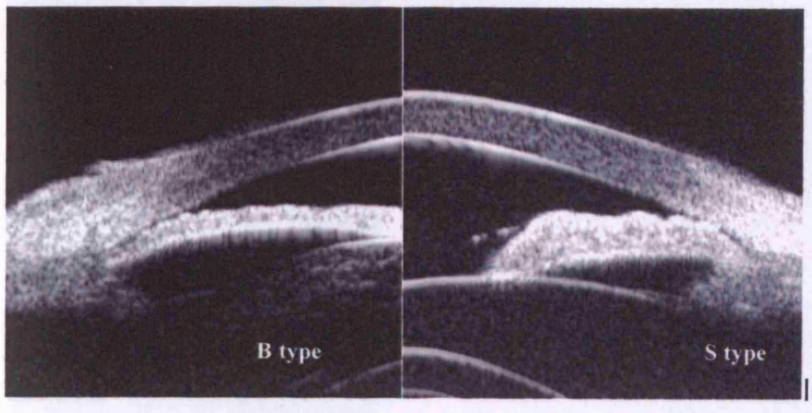
Figure 18: Iris thickness at basal part close to the iris insertion: thin, medium and thick, classification as for overall iris thickness.



Iris TM contact: None

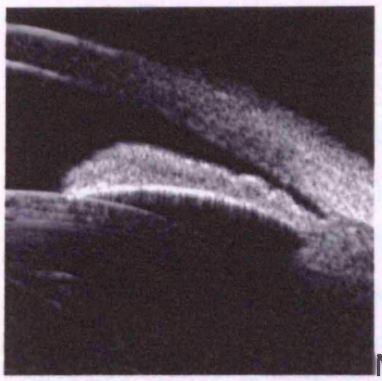


Iris TM contact: Low

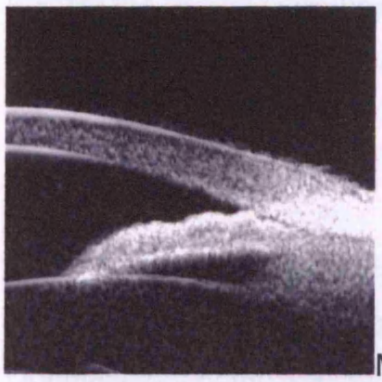


Iris TM contact: High

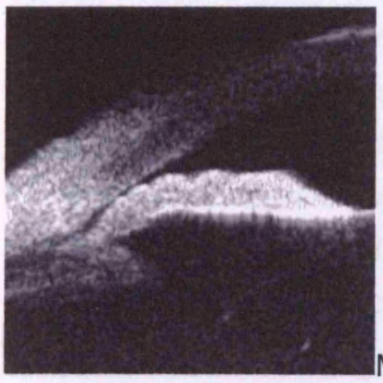
Figure 19. Appositional closure is classified according to the height of iris-TM contact. Two kinds of appositional closure are currently recognised when iris-TM contact is high: B type (contact starts from the bottom of the angle recess); S type (contact occurs at the level of the scleral spur with an aqueous filled space, "Mapstone's sinus", between peripheral iris and TM posterior to this).



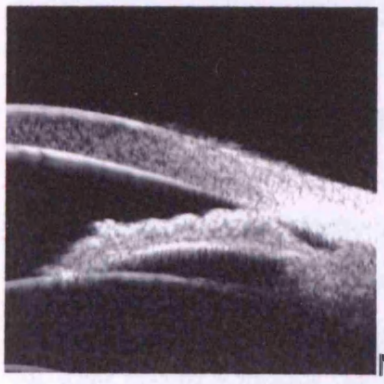
Mapstone sinus: not applicable



Mapstone sinus: Absent



Mapstone sinus: Slit



Mapstone sinus: Wide

Figure 20. Mapstone sinus (the space posterior to the iris-TM contact) is classified if the iris-TM contact is high.

Reproducibility of image acquisition by the same examiners was assessed using images acquired from all four quadrants of one eye of 34 subjects (16 narrow angles and 18 normal angles), on two separate occasions. Reproducibility of image analysis by the same observer was similarly examined by making measurements on the same image on two separate occasions. In the assessment of reproducibility of image analysis, the observer was required to identify the scleral spur (used by the analytical software as the cardinal landmark in making measurements) on two separate occasions.

2.4 Study of the effect of laser iridotomy

2.4.1 Patient selection and informed consent

This prospective study was approved by the Ethics Committee of Zhongshan Ophthalmic Center. Patients confirmed to have at least 270 degrees of angle circumference in which the posterior (usually pigmented) trabecular meshwork was not visible during static gonioscopy, and also completing UBM examination, were enrolled. Provocative testing was not required as an enrollment criterion for this treatment. Any conditions precluding follow-up (severe health problems, etc) and clear visualization of the drainage angle (corneal opacity, etc) were considered grounds for exclusion. Written, informed consent was obtained after carefully explaining the potential side effects and benefits of the project in detail. The current study examined short-term post-laser results.

2.4.2 Treatment procedures

Laser peripheral iridotomy was performed using both the argon and YAG lasers in one, randomly selected, eye if the patients presented with bilateral occludable angles. The primary investigator (MHE) performed LPI. One drop of pilocarpine 1% was instilled fifteen minutes prior to treatment. It was required that the pupil size be less than 2 mm. Location for the treatment in the superior region (from 10:00 to 2:00) at the peripheral 1/3 of the iris where the iris appeared thinnest. The argon laser was used starting at settings of 500 to 1000 mW with a spot size of 50μ for duration of 0.1~0.3 seconds. The energy level was adjusted according to the tissue response. Once iris appeared to be honeycomb-like or the iridotomy

was near complete, the YAG laser was used starting at an initial setting of 2 – 6 mJ, until the iris was fully perforated. An iridotomy of about 0.3 mm was the objective. Full thickness perforation was confirmed once an aqueous plume with dispersing pigment was seen. All iridotomies were performed using an Abraham lens to focus the laser beam. The baseline IOP, number of shots and energy setting used were recorded. Individuals who had an IOP rise less than 5 mmHg 1 hour after the treatment were discharged. Otherwise, subjects were given topical carbonic anhydrase (Trusopt, Merck & Co. Inc. NJ, USA) and 0.5% Timolol, and IOP was re-checked one hour later. If IOP had not risen further during the next hour, the patients were discharged. All the discharged patients were given 0.1% Dexamethosone drops four times a day for a week and asked for return for postoperative examination in two weeks time. Pilocarpine was not used after the treatment.

2.4.3 Post-Laser Examination

At 2 weeks after the laser PI patients were asked to return for a further examination. These examinations included: visual acuity, IOP, gonioscopy, traditional and modified slit lamp oblique flashlight test, van-Herick test and UBM examinations. The clinical protocol was identical to that described above.

2.5 Data management and statistical analysis

Examination sheet was checked for completeness before the patients left the examination site. Fundus photos were scanned and digitalized. UBM data were stored on Magento-Optical drive initially, and copied to the hard disc of a personal computer for storage, with appropriate back-up. Hard and soft copies of visual field results were scanned and stored on the hard disc of a personal computer.

EpiInfo for Windows 2000 (released at 2003-11-17) was used for data entry. A simple programme was generated and used for data entry. Double entry was not conducted. Comprehensive data cleaning was conducted by checking the range and consistency of the data.

2.5.1 Prevalence survey

Age and gender-specific prevalence was calculated using the number of cases (based on glaucoma definition described above) as the numerator, and the number of subjects examined as the denominator. Confidence interval at the 95% level was calculated by Poisson distribution but clustering effect was not adjusted. Other confidence interval was calculated assuming normal distribution using Stata Package (Stata 8.0; Stata Corp., College Station, TX).

3. Results

3.1 Population survey in Liwan District, Guangzhou

3.1.1 Characteristics of the examined and enumerated population

In Fengyuan street block, 2,313 subjects aged 50 to 102 years at the time of examination were identified from 1,569 households using the Household Resident Register. The number of eligible subjects in each household ranged from one to four. Of these, at the time of door-to-door enumeration, 19 had died and 430 had either moved from their original residence or their houses had been demolished prior to redevelopment. These subjects were considered ineligible and were excluded from the study. Those who were severely ill were still considered eligible for examination. **Table 6** compares the demographic characteristics of the enumerated sample with those of the sampling frame (Fengyuan street block) and the total population of the district (the demography for the latter two are based on data from the 2000 National Census). Subjects aged 60-69 years were under-represented in the sample, but otherwise, the demography in these 3 populations was similar.

Among the 1,864 eligible subjects, 1,405 (75.3%) were successfully examined. Nineteen subjects were examined in their own homes. **Table 7** summarizes the age-specific response rates and demographics of the examined subjects. The men aged 50-59 years (response rate 63.6%) and those aged 80 years and older (response 59.5% male, 60.4% female) had disproportionately lower response rates. The response rate in women was higher than for men (men: 76.2%; women: 79.2%, X^2 test, P<0.001).

3.1.2 Prevalence of blindness and glaucoma

Table 8 summarizes the distribution of vertical cup:disc ratio (VCDR) in right and left eyes of the subjects after excluding the cases with definite glaucoma. The distribution of VCDR in right and left eyes was similar, with 0.4 as the median, 0.7 and 0.8 as the 97.5th and 99.5th percentiles. As for the absolute difference of the VCDR in right and left eyes, the mean, 97.5th and 99.5th percentiles for this

asymmetry were 0, 0.2 and 0.3 respectively. These percentile figures were used as cut-off values in the category 1 and category 2 in the diagnostic definitions of glaucoma. Eighty-seven right eyes (6.2%) and 94 left eyes (6.7%) did not have valid data for VCDR mainly because of the poor visualization of the disc due to media opacity. **Table 9** summarizes the distribution of intraocular pressure (IOP) measured by Tono-pen tonometer after excluding the definitive glaucoma cases. The IOP distribution in right and left eyes were generally similar, with mean, median, 97.5^{th} and 99.5^{th} percentile as 15, 15, 21 and 24mmHg respectively. The 99.5^{th} percentile (24mmHg) was used as the cut-off value for the category 3 definition. IOP values were missing in 27 right and 28 right eyes (2%) mainly because of the corneal pathology and patients who could not cooperate.

Figure 21 shows the distribution of IOP in right eyes for all subjects. **Table 16** summarizes the IOP level in age decades and gender. The mean IOP in this group of adult Chinese was 15.2 mmHg (95%CI: 15.1~15.4 mmHg; SD: 3.1 mmHg). Multiple linear regression model using age and gender as independent variables suggested the IOP was lower in older people, with an overall 0.2 mmHg decrease in mean IOP in each decade age-group (β =-0.2, P=0.004). IOP was 0.37 mmHg lower in women than men (P=0.025).

One hundred and eighty-three subjects had VCDR $\geq$ 0.7 in either eye or asymmetry $\geq$ 0.2 (14.2% of those with available VCDR data). Of 125 right eyes meeting these criteria, stereo disc photography was available in 85 eyes (68.5%), similarly in the left eyes. These stereo photos were used to verify the diagnosis by the review of disc photos, visual field data and other clinical data including IOP and visual acuity.

Overall 42 (23.0%) of those who met the above VCDR criteria did not complete a satisfactory visual field test in both eyes. Among these, 7 individuals had poor vision, mainly because of cataract, 9 individuals were too frail to complete the test (> 80 years). A total of 9 individuals were diagnosed as suffering glaucoma in these 42 cases without visual field results, based on category 2 or 3 definitions.

Fifty-three people were found to have glaucoma (**Table 10-11**). Twenty-nine

(54.7%) had POAG, 21 (39.6%) had PACG and 2 (3.8%) had secondary glaucoma (1 neovascular, 1 traumatic). It was not possible to classify the mechanism in 1 case because both eyes had undergone cataract surgery, and diffuse board PAS were seen. Consequently, objective classification on the angle width was not possible. In the 21 PACG cases, 13 were unilateral and 8 bilateral PACG cases. Eight cases (38%) had a history of an acute, symptomatic attack. Twelve (57%) had been diagnosed or previously operated. Nine cases (43%) were blind in at least one eye, but none were bilateral blind. On the other hand, in 29 POAG cases, only 2 (7%) cases had been diagnosed and operated on previously. Five cases were blind in one eye (17%). One of these was a highly myopic eye (spherical equivalent=-20D). **Table 12** lists the major findings in definite glaucoma cases.

Table 11 summarizes the number and diagnostic category of all glaucoma cases, and gives the age-specific rates. The crude prevalence of glaucoma was 3.8% (95%CI: 2.8~4.8%). Using the Guangzhou census data as the standard population, the age- and sex-standardized prevalence of glaucoma was 2.7% in people aged 50 years and older. The crude prevalences of POAG and PACG were 2.1% (95%CI: 1.4~2.8%) and 1.5% (95%CI: 0.8~2.1%) respectively. The prevalence of all glaucoma increased significantly with age. Glaucoma occurred predominantly in men. In a logistic regression model, the adjusted ORs for 60-69, 70-79 and 80+ versus the 50-59 years were 2.9 (95%CI: 1.1~8.4), 5.6 (95%CI: 2.1~14.8) and 13.1 (95%CI: 4.6~37.8) respectively. Women had a lower odds than men [Adj. OR: 0.5, 95%CI: 0.3~0.8].

Suspect primary angle-closure ("occludable angles") (**Table 13**) was defined by the pigmented trabecular meshwork not being visible in at least 3 quadrants in either eye. This was identified in 10.2% (95%CI: 8.6~11.8) of subjects. This rate includes any occludable angle solely based on the gonioscopic grading irrespective of the PAC and PACG diagnosis. The prevalence was almost twice as high in women (12.5%) compared with men (7.1%). This prevalence increased with age, from 3.7% in 6th decade to 20.0% in 9th decade. Among the 140 cases diagnosed as angle-closure suspects, 74 were bilateral and 66 were unilateral. Unilateral angle-closure suspects were identified because they met the specific cut-off used (the number of quadrants without pigmented trabecular

meshwork visible) in the definition rather than suggesting significant asymmetry of the gonioscopic angle width.

Prevalence of angle closure was decided based on the individual (either eye of the individual); The diagnosis was made when the particular characteristics was identified in either eye. The diagnosis was made according to the eye with more severe form if the disease status was different in two eyes. For example, when the cases presented with suspect angle closure in one eye and with PAC in the other eye, a diagnosis of PAC, instead of angle closure suspect, was made. Prevalence rate for primary angle closure suspects refers to all occludable angles cases found by gonioscopy (including PAC and PACG eyes).

PAC was identified in 2.4% (95%CI: 1.6~3.1) of subjects. The prevalence was three times higher in females (3.3%) than males (1.1%) and, in general, increased with age. The prevalence of PAC in 50-59 years was low, 0% in men and 1.9% in women. Among the total 33 PAC cases, 3 people had suffered a previous acute episode, but had normal disc and field. All PAC cases had PAS in either right or left eye, except for one who had suffered an acute episode but had been left without PAS.

Primary angle closure glaucoma was diagnosed in 21 cases (1.5%, 95%CI: 0.9~2.1). Among them, nine cases had elevated IOP ($\geq$ 21mmHg) at screening and 10 cases with normal IOP following glaucoma surgery. The remaining 2 cases had normal IOP on the screening examination and had not received glaucoma treatment. These 2 cases were diagnosed on the basis of glaucomatous field and disc damage, combined with gonioscopically occludable angles; one had PAS, the other did not. There were 8 cases (38%) that had previously been symptomatic. The prevalence of PACG increased with age and was higher in females (13 cases, 1.6%) than males (8 cases, 1.3%) although this difference was not statistically significant (Chi square test, $P>0.05$).

Table 14 and **Table 15** summarize the number of cases of unilateral and bilateral blindness, based on presenting and best corrected visual acuity. Considering presenting visual acuity (with subjects' own correction if worn), 82 individuals (5.9%) had at least one eye blind, and only 7 cases (0.4%) were bilaterally blind.

The leading causes of blindness in at least one eye were cataract (37.8%), glaucoma (12.2%) and myopic retinopathy (11.0%). The 7 bilaterally blind cases included 2 cataract, 1 glaucoma, 2 pigmentary retinopathy, 1 uncorrected myopia with myopic retinopathy and 1 diabetic retinopathy. Considering best corrected visual acuity, the number of cases of blindness fell to 67 (4.8%) and 6 (0.4%) in at least one eye and both eyes respectively. The leading causes for those with at least one eye blind were cataract (43%) and glaucoma (15%). The causes for bilateral blind were similar.

3.1.3 Biometric characteristics of the globe

3.1.3.1 Axial anterior chamber depth (ACD)

Table 17 summarizes the axial anterior chamber depth in the right eye measured by optical pachymetry in the subjects after excluding 47 aphakic and pseudophakic eyes. The ACD was calculated by subtracting the corneal thickness measured by Instrument I (Haag Streit optical pachymeter). The ACD therefore represents the distance between anterior capsule of the lens and the endothelial layer of the cornea in the pupillary axis. ACD data were missing in 110 right eyes, mainly because this examination was not performed for every subject in the first 3 days of the examination period and a few subjects who were not fit enough to undergo this examination (because of Parkinson syndrome, paralysis, etc).

The mean ACD values for men and women were significantly different: 2.59 mm (95%CI: 2.56~2.62) and 2.42 mm (95%CI: 2.39~2.44) respectively (t test, $P<0.001$). Overall, older subjects had a shallower ACD, among both males and females. **Figure 22** plots the centiles of the ACD against the centiles of normal distribution, suggesting the ACD distribution is close to normal distribution. The Lowess curve gives a representation of central tendency of the data without imposing a specific mathematical model. Multiple linear regression of ACD on age and sex ($R^2=0.14$, $P<0.001$) suggested that mean ACD declined by 0.09mm (95%CI: -0.011, -0.008) per decade (adjusted for sex) and was 0.177 mm (-0.213, -0.141) shallower in women than men (adjusted for age). The

regression coefficients of ACD with age in males and females were -0.010 (P<0.001) and -0.009 (P<0.001). **Figure 24** illustrates a quadratic regression curves for the two sexes, suggesting a similar cross-sectional pattern of decrease in ACD values with age. Adding the spherical equivalent (SE) value of refraction to the regression model, the variation in ACD was better explained, with an R^2 of 0.21 and the regression coefficient for SE was -0.030 (95%CI: -0.036, -0.023)

3.1.3.2 Lens thickness

Ultrasound biometry data were not successfully collected in 103 subjects because the measurement was not performed on all subjects in the first week of examination. In addition, measurement was impossible during home visits (19). Forty-seven people had undergone cataract surgery and were consequently excluded from the analysis. **Table 18** summarizes the lens thickness in decade age and sex categories. The mean lens thickness was 4.27mm (95%CI: 4.23, 4.31), 4.22mm in men and 4.31mm in women. Frequency distribution plot suggests the distribution of lens thickness did not conform to a normal distribution (**Figure 25**). **Figure 26** gives the Lowess curve of lens thickness with age by men and women. Because the association with age was not linear, box and whisker plots rather than scatter linear plots were used. The box-plots of lens thickness (**Figure 27**) illustrate that the older subjects had thicker lenses, and that women tended to have thicker lenses than men according to the median values (P<0.001).

3.1.3.3 Axial length

Similarly, axial length (AL) data was obtained by ultrasound biometry with the same availability of data as for lens thickness. **Table 19** summarizes axial length by age and sex. **Figure 28** confirmed the distribution of axial length did not conform to a normal distribution, and was skewed towards longer axial lengths. Lowess smoothed distribution plots do not support the existence of differences in AL between age-groups in men or women (**Figure 29**). **Figure 30** suggests that axial length does not change with age but women have a shorter axial length than men. Multiple linear regression models (assuming normal distribution) tell the same story (R^2: 0.03, P<0.001); age was not significantly, linearly associated

with axial length (Beta: 0.0001, P=0.97). However, women had a 0.50mm shorter eyeball than men (Beta: -0.503, P<0.001). A non-parametric rank sum test also detected the same sex difference (Mann-Whitney two-sample, Z=9.11, P<0.001). However, when adding the spherical equivalent value into the linear regression model, the variation explainable by the variables significantly increases to 52% (R square: 0.52, P<0.001), and the spherical equivalent value becomes highly significant, suggesting axial length increased 0.3 mm with the SE increasing 1 dioptre toward the myopia.

3.1.3.4 Relative lens position

Relative lens position (RLP) was developed by Lowe as an indicator of risk of angle-closure, taking ACD, lens thickness and axial length into account. **Table 20** presents the RLP by age and gender. A multiple linear regression model did not detect any significant linear association with age or gender. The linear regression model constructed, using age and sex as independent variables, was itself not significant (R^2: 0.0009, P=0.556).

3.1.3.5 Corneal thickness

Ultrasound central corneal thickness was reported in **table 21** in the phakic subjects. Linear regression model (R square 0.014, P=0.0002) suggests the ultrasound corneal thickness decreased with age (Beta: -0.4 mm per age, P<0.001) but not significantly associated with gender (Beta: -0.5 for female versus male, P=0.803).

3.1.4 Gonioscopic angle characteristics

3.1.4.1 Agreement on gonioscopic examination

Gonioscopy was one of the key outcome variables in this study. It was performed on all subjects. For quality control purposes, the concordance between the examiner (MH) and another experienced gonioscopist (PJF) was tested on the left eye of 28 consecutive subjects during the pilot phase. Because the majority of the cases did not have occludable angles, it was not possible to compare agreement on the identification of occludable angles. The agreement in the Shaffer grading of angle width in superior and inferior quadrants was tested

using weighted kappa values. Weighted kappa values for Shaffer grades of superior and inferior quadrants were 0.63 (SE:0.18) and 0.62 (SE:0.25) respectively. The superior quadrant grades by PJF (mean=2.59) were narrower than MHE (mean=2.81) but this difference was not statistically significant (Wilcoxson rank test, P=0.31). Differences in grading the inferior quadrant were similar. The weighted Kappa values for the Spaeth apparent iris insertion grading on superior, inferior, nasal and temporal quadrants were 0.69 (SE:0.24), 0.84 (SE: 0.37), 0.71 (SE:0.35) and 0.77 (SE: 0.29) respectively.

Gonioscopy was carried out before the optical pachymetry and ultrasound biometry, and the examiner was therefore masked to the axial ACD value of the subjects.

3.1.4.2 Gonioscopic angle width

Gonioscopy data was not available for 30 subjects. Among these, the reasons for the missing data were: examination at home preventing gonioscopy 16, refused 2, unable to tolerate examination 4, corneal opacity 4 and other reasons 4.

Following the exclusion of 47 subjects who had undergone previous cataract surgery, **Table 22** presents the angle width characteristics by age and gender. The angle width was significantly less in women than men in both superior and inferior quadrants (t test, $P<0.001$). Superior quadrants had a significantly narrower angle width than inferior (Wilcoxon Signed-rank test for paired comparison, $P<0.001$). When the average width of angle (in superior and inferior quadrants) was analyzed as a continuous variable and by using a multiple linear regression model, (R^2: 0.156, $P<0.001$), the angle width was significant narrower in the older people, with a 0.4 grade difference in observed mean angle width for each 10 years of age (ß: -0.042, $P<0.001$) and a 0.5 grade difference between women and men (ß: -0.505, $P<0.001$).

3.1.4.3 Level of apparent and true iris insertion

Table 23 summarizes the age and sex-specific proportions of iris insertion grades during static gonioscopy of right eyes. The data on superior and inferior

quadrants were arbitrarily selected to present the data in this table. The overall proportion of Grade A, B, C, D, E in the superior quadrants were 8.5%, 18.7%, 40%, 28.0% and 4.8% respectively. These proportions were 1.4%, 6.3%, 45.3%, 41.1% and 5.9% respectively for the inferior quadrant. The proportion of relatively anterior insertions (Grade A to C) increased with age (Chi square test, P<0.001) and tended to be higher in women than men (men: 59.0%, Women 72.5%, Chi square test, P<0.001).

Table 24 gives the rate of narrow (judged "occludable") angles, defined as those where the posterior (usually pigmented) trabecular meshwork was not visible (Grade A and B).

Table 25 gives the age and sex specific proportions of true level of iris insertion on *dynamic* gonioscopy. The proportion of Grades A and B in both superior and inferior quadrants decreased to less than 1.5% from over 20% during *static* examination. True iris insertions were on the ciliary body (Grade D and E) in most of the subjects (62.2% superior, 79.5% inferior). The proportion of anterior insertions (Grade A, B or C) increased with age from 25.7% in 6^{th} decade to 54.9% in 9^{th} decade at the superior quadrant. A trend of increasingly anterior iris insertion in the inferior quadrant was also seen. Females had a more anterior insertion than men with a proportion of Grades A, B and C in the superior quadrant of 40.5% compared with 31.1% in males (Chi Square test, P<0.001).

3.1.4.4 Iris profile

Table 26 summarizes the iris profile by age (decades) and sex. The proportion of steep profiles was higher in women than men (X^2=52.9, P<0.001). The proportion of steep profiles increased with age, from 19.3% in 6^{th} decade to 47.7% in 9^{th} decade (Chi square, P<0.001). However it was noted that this proportion decreased in 9^{th} decade female group. The proportion of concave profiles was higher in men but was not associated with age. Plateau iris configuration was more common in women (11.6%) than men (8.1%,P=0.033). Using multiple logistic regression to examine the association between iris profile, age and sex, the adjusted OR of a steep profile increased ; 2.19 (P<0.001), 3.48 (P<0.001) and 3.79 (P<0.001) among people aged 60-69, 70-79 and 80 years

and older respectively, compared with those aged 50-59 years. Women were twice as likely as men to have a steep iris profile (OR: 2.14, P<0.001, adjusted for age). The pattern was repeated among those with a plateau iris profile. The odds ratios (adjusted for sex) for people aged 60-69, 70-79 and 80 years and older (versus aged those 50-59 years) were 3.05 (P<0.001), 3.36 (P<0.001) and 3.94 (P<0.001). In women, the odds of a plateau iris configuration were 48% greater than in men, after adjustment for age differences (OR: 1.48, P<0.001).

Table 27 gives the proportion of iris profile grades sub-divided by Shaffer angle widths. The proportion of people with steep iris profiles increased from 3.2% in Grade 4 to 70.6% in Grade 0. The proportions of plateau profile were generally low in eyes with wide angles (Shaffer grades 3 and 4), but increased among those with grade 0 or 1 to affect about 1/3 of subjects.

3.1.4.5 "Occludable" angles on gonioscopy

The definition of an "occludable angle" is, to a certain extent, arbitrary. However, it does suggest greater possibility of angle-closure. We used two criteria to define an occludable angle: one (Definition 1) is a more stringent criterion used in previous surveys, where the posterior (usually pigmented) trabecular meshwork is not visible in at least 3 quadrants during gonioscopy without indentation. Another criterion (Definition 2), however, is more liberal, stipulating 2 or more quadrants without visible posterior/pigmented TM as the cut-off. Definition 2 was used as the selection criterion in the current study to classify cases and controls for the UBM examination and laser PI treatment.

Table 24 presents gonioscopic data on the age and sex-specific proportions of people with angles without visible posterior TM (Grade A or B apparent insertion) in each of the 4 quadrants, The proportion of eyes with irido-trabecular contact was different in the 4 quadrants: superior > (nasal = temporal) > inferior. The proportion of narrow angles increased with age and was higher in females. Using logistic regression, the adjusted OR's for having a narrow angle in the superior quadrant in people aged 60-69, 70-79 and 80 years and older, compared with those aged 50-59 years were 2.94 (P<0.001), 4.17 (P<0.001) and 4.97 (P<0.001). The age-adjusted OR was 2.00 in women relative to men

(P<0.001). The most pronounced increase in this proportion was between the 6th decade (5.4%) and the 7th (24.4%) in men.

3.1.4.6 Peripheral anterior synechiae (PAS)

A total of 54 right eyes (3.9%) and 49 left eyes (3.6%) were found to have PAS. Among these, 19 (35.2% of the total) right eyes and 20 (40.8%) left eyes were associated with previous cataract surgery. About half of the aphakic or pseudophakic eyes had some PAS (42.2% right, 50.0% left). In right eyes, after excluding aphakic and pseudophakic eyes, PAS were found in 29 out of 146 (19.9%) eyes with occludable angles (defined as the posterior TM not being visible in 3 or more quadrants), and only 6 in 1,184 (0.1%) eyes with an angle that did not meet the definition of "occludable". **Table 28** summarizes the gonioscopic features of cases with PAS. The percentage of PAS dramatically increased from 1.9% (95%CI: 0.4~3.8) in Shaffer grade 2 to 12.6% (95%CI: 7.1~18.1) in Grade 1 and 27.5% (95%CI: 14.8~40.1) in Grade 0. Similarly, the percentage of PAS increased significantly from 4.6% (95%CI: 0.1~9.1) in eyes with posterior (usually pigmented) TM being not visible in 2 quadrants to 15.2% (95%CI: 7.7~22.7) if in 3 quadrants and 29.6% (95%CI: 17.0~4.2) if not visible in 4 quadrants. This suggests that the incremental changes in features identified on gonioscopic examination are linked with an increased rate of an examiner identifying structures that are classified as PAS. This pattern also supports the belief that the grading systems used to classify angle configuration (Shaffer angle width and the number of quadrants with visible posterior TM) do reflect a change in the risk of angle-closure.

Two right eyes and 3 left eyes had wide angle and PAS but had not undergone cataract surgery. In 2 of these, the cause was not identifiable. In 3 there were signs of previous trauma and 1 was a watch-maker who habitually wearing lens attached on the eyelid, this attached lens may inert pressure on the limbus and causes subsequent PAS.

3.1.4.7 Factors associated with angle width

Table 29 summarizes the association between mean Shaffer angle width and

ocular biometric parameters, corneal curvature, refractive status and BMI index and height. In a linear regression model, adjusted for age and gender, all variables (shorter ACD, thicker and anterior located lens, shorter axial length, more hyperopic refraction, smaller BMI ($P<0.001$ in all) were associated with narrower Shaffer angle width. The one exception was the corneal curvature was not significantly associated ($P=0.33$). In a regression model incorporating a single biometric variable, the greatest variation in angle width explained by the variation of independent variable was found in ACD, age and gender model (R^2: 0.52). Most of these variables were co-linear, it was therefore not possible to pool all the variables into a multiple regression model.

3.2 Case control study

In an attempt to examine potential screening tests which may aid the rapid identification of high risk eyes, and to gather more data on the characteristics of eyes with angle-closure on ultrasound biomicroscopy relative to the unaffected population, it was decided to recruit subjects to a nested case-control study.

3.2.1 Data availability

As described above in the Method section, the selection criterion for the cases was based on static gonioscopy, specifically, where the posterior (usually pigmented) trabecular meshwork was not visible in at least 2 quadrants. Controls were selected by systematic random sampling (1 person in every 10 examined) in those *not* meeting the criteria for "cases". Cases with PAC and PACG were excluded from the analysis. Cases with previous cataract surgery were excluded also. Right eyes were arbitrarily selected for presenting the comparison. The right eyes meeting the criteria of narrow angle by *Definition* were classified as ***"cases"*** (194 cases), the remaining eyes were considered ***"controls"*** (122 cases).

3.2.2 Demographic and biometric characteristics in cases and controls

Table 30 summarizes the demographic characteristics of cases and controls. Cases tended to be older than controls ($P<0.001$). The proportion of women was

greater in cases group (P=0.084). Cases tended to be more hyperopic (14.7% of cases versus 3.6% of controls, P=0.006). Intraocular pressure was not significantly different in these two groups. The means of 15.1 mmHg in both groups were close to the mean IOP in all subjects. The *cases* group tended to be lighter in weight (P=0.008), shorter in height (P=0.011) and had a lower body mass index (P=0.095). However, by logistic regression, neither weight nor height were significant factors for being classified as angle-closure suspects, after controlling of age and sex.

Shallower ACD, shorter axial length and thicker lenses were found in the case group (**Table 31**). These differences were all statistically significant (P<0.0001). Relative lens position was more posterior (i.e. a higher ratio) in the control group (P=0.008). There was no significant difference in corneal curvature (P=0.92).

3.2.3 Gonioscopic characteristics in cases and controls

Gonioscopy data was available for all subjects in the case-control study. **Table 32** shows the gonioscopic findings in cases and controls. The comparison was not carried out for apparent iris insertion as this was the classification criterion. After excluding 6 subjects with aphakic or pseudophakic eyes from the control group, the cases tended to have a narrower Shaffer angle width in both superior and inferior quadrants (P<0.001). True iris insertion was more anterior located in cases group. The proportions of eyes with a true iris insertion at the scleral spur (Grade C) were 87.6% in cases and 34.8% in controls (P<0.001) at the superior quadrant. The situation in the inferior quadrant was similar. Steep and plateau iris profiles were more common in the cases than controls (P<0.0001). However there were still 35% of "normal" controls with a steep iris profile. The proportions of four types of iris profile in controls group were similar to the overall examined population except the proportion of plateau profile was slightly lower.

3.2.4 Efficacy of conventional and modified screening examinations in case-control study subjects

Table 33 gives the proportion of deep, medium and shallow grades by traditional oblique penlight test. In the eyes classified as having occludable angles, about

79% of them were classified as Shallow in this scheme. About 20% of normal (being not occludable) were classified as Shallow. The proportion of the "Shallow" category was significantly higher in cases group (P<0.001). Using this category, the sensitivity and specificity for identification of occludable angles were 78.7% and 80.2%. In Receiver Operation Characteristic (ROC) statistics, the area under ROC curve was 0.826 (95%CI: 0.778~0.874) (**Figure 32**).

The oblique test was repeated using a slit lamp eyepiece measuring graticule to exactly measure the full length of the light band and shadow was also performed (**Table 34**). The band length, corresponding to the corneal diameter, was significantly smaller in cases (P=0.05). The length of iris shadow was longer in cases (P<0.001). The median of the ratio of shadow versus band length were 0.20 in cases and 0.13 in controls. This ratio in the cases group was equivalent to 1/4 of the corneal diameter and was located close to the mid-point of the nasal iris. The area under ROC curve was 0.888 (95%CI: 0.852~0.924). The sensitivity and specificity were 84.8% and 76.7% if a cutoff of 0.18 was used, and changed to 91.4% and 71.4% with the cutoff at 0.20, and 69.5% and 91.4% if the cut-off was changed to 0.15.

Figure 35 compares the ROC curves for optical and ultrasound ACD measurement for detection of occludable angles. The cutoff value at which sensitivity and specificity were approximately equal (82% and 81% respectively) for optical ACD was 2.27mm. For ultrasound ACD it was 2.53mm with a sensitivity of 73% and specificity 71%. Area under the ROC curves was 0.896 for optical pachymetry and 0.797 for ultrasound. Taking the all the subjects rather than just the cases/controls group, the area under ROC curve was 0.921 for optical ACD (N=1,243) and 0.803 for ultrasound ACD (N=1,252). The sensitivity and specificity for optical ACD were 88% and 83% when a screening cut-off of 2.27 mm was used, and for ultrasound ACD, the values were 75% and 73% with a cutoff value of 2.53mm.

Table 35 gives the proportion of van Herick results (graded with reference to standard photos) in cases and controls. The proportions with a shallow peripheral chamber ($\leq$ 15% of the corneal thickness) were 81.9% among cases and 13.4% in controls. The ROC statistics indicate an area under the curve of

0.907 (95%CI: 0.870~0.944). The sensitivity and specificity were 81.9% and 86.5% with a cut-off of limbal chamber depth = 25% CT.

Table 36 compares data from cases and controls when a slit lamp eyepiece graticule was used to measure limbal chamber depth by the van-Herick technique. The mean peripheral corneal thickness was statistically thinner in case group than in controls (t test, P=0.045). The peripheral anterior chamber depth in cases was significantly shallower than controls (2.6 versus 6.6 units, t test, P<0.001). Cases had a smaller peripheral chamber depth to corneal thickness ratio (0.22 versus 0.54, t test, P<0.001). In ROC statistics, the area under the curve was 0.901 (95%CI: 0.861~0.940). The sensitivity and specificity were 83.6% and 81.9% when the cutoff was chose at 0.33.

3.2.5 Characteristics in PAC and PACG eyes.

A total of 33 cases were diagnosed as PAC individuals and 21 cases identified to be PACG cases. In order to describe the characteristics, only the right eye was chose for the comparison. A total of 26 and 16 right eyes had PAC and PACG respectively. The mean age was older in PAC (68.7 years) and PACG (72.9 years) compared to the normal controls (65.2 years). The mean of ACD in PAC was 1.98 mm (95%CI: 1.88, 2.09) and in PACG was 2.06 mm (95%CI: 1.69, 2.42) compared to 2.05 mm (95%CI: 2.00, 2.09) in angle-closure suspects and 2.58 mm (95%CI: 2.56, 2.61) in normal controls. Consistently, the mean Shaffer grade in the inferior quadrant was found 0.8 in both PAC and PACG compared to 1.2 in angle-closure suspects and 3.2 in normal controls. However, one must be cautious as drainage angle width may have been changed by glaucoma surgery in the PAC or PACG eyes. The small number of cases with PAC and PACG hinders a meaningful comparison between these groups, for instance, the control of age and sex.

All PAC eyes had PAS at presentation except one case with a history of an acute episode that had subsequently undergone a laser iridotomy. Early PAS were found in one case; the PAS divided after dynamic gonioscopy (**Figure 36**). PAS were found most frequently in the superior quadrant. Two subsequent figures illustrated the morphology of PAS with clear border (**Figure 37**) or with a gradual

increase and decrease of the height of PAS (**Figure 38**). Isolated, small PAS were also found in 2 cases (**Figure 39**).

3.3 Ultrasound biomicroscopic (UBM) findings

3.3.1 Attendance of the subjects for UBM examination

A total of 119 (63.9%) participants with narrow angles and 68 (57.7%) controls were successfully examined by UBM. The major reasons for not attending the UBM examination were refusal, or the subject being unsuitable for examination (e.g. due to paralysis or other physical disability for example).

Table 37 summarizes the demographic and biometric characteristics of those who did and did not present for UBM examination. From inspection, those who attended the UBM examination tended to be younger. The attendance rate for age 50-59 was 75.0% and decreased to 26.0% in 80+ age group among the cases. Our experiences in arranging the tests suggested that reasons for non-participation of older people were mainly lack of interest in undergoing further diagnosis and treatment, as well as physical limitations to mobility, although free transportation to the main ZOC hospital was offered. There was a non-significant trend among women to have higher attendance rates than men (X^2: 0.19, P=0.66). The ACD (P=0.55) and Shaffer angle width grades (P=0.12) of the attendees and absentees did not differ, suggesting the overall angle status in the attendees and absentees was similar.

3.3.2 Reliability of UBM quantitative measurement

Reproducibility was evaluated in 34 eyes with repeated image acquisition on each quadrant. **Table 38** presents the results of repeated analysis on the same image, and of repeated image acquisition at the same location. Data for angle width, iris thickness and iris curvature are summarised.

3.3.2.1 Reproducibility of angle width measurement

Anterior opening distance (AOD) at two distances, 250 and 500 microns, from the scleral spur were evaluated. In terms of repeated image acquisition at the

same quadrant, reproducibility tended to be poorer on AOD250 compared to AOD500, with wider 95% limits of agreement. The angle width measurements in the superior quadrant tended to have poorer reproducibility than the other quadrants. The variation in measurements derived from repeated analysis of the same images tended to be smaller than that observed when different images of the same structures were measured. In repeated measurements on the same image, the difference between two measurements was only significant for AOD500 in the temporal quadrant's (diff=0.014, $P<0.05$, t test). The 95% limits of agreement suggested the variation in both AOD250 and AOD500 were similar, e.g., -0.041~+0.040mm for AOD250 and -0.032~+0.034mm for AOD500 at superior quadrant.

3.3.2.2 Reproducibility of iris thickness

The iris thickness measurements at 750 microns from the scleral spur were used to assess reproducibility. We hypothesized that the variations attributable to image acquisition and image analysis may both exist Reproducibility was poorer for the inferior quadrants, as suggested by 95% limit of agreement (-0.139~0.131). Mean of difference was significant only for the inferior quadrant when the same image was repeatedly analyzed (diff=-0.036, $P<0.05$, t test).

3.3.2.3 Reproducibility of iris curvature

Iris curvature was calculated as the radius of the curvature. There was no significant difference in means of both repeated analysis and repeated image acquisition, except in the case of repeated image acquisition in the superior quadrant (diff=5.382, $P<0.05$, t test).

3.3.3 Range of UBM measurements in normal subjects

UBM examination was successfully performed on 68 normal "control" subjects. Q-Q plot suggested that the variables angle width, iris thickness and TCPD in the normal subjects conformed to approximate normal distributions when comparing the quantiles of the variables against the quantiles of the normal distribution (figure not shown).

3.3.3.1 Angle width at 250 and 500 microns to scleral spur

Table 39 and **table 40** shows the mean and SD of major UBM measurements in four quadrants for this group of normal subjects. Mean angle width at 250 microns (AOD250) and at 500 microns (AOD500) from the scleral spur increased in the order superior < inferior < nasal with the temporal quadrant consistently being the widest, suggesting the angle width indicated by UBM was narrower in superior and inferior quadrants than temporal and nasal quadrants. Measurements of angle recess area (ARA) at 750 microns from the scleral spur show a similar trend. The narrowest angle being found in the superior quadrant agrees with gonioscopic findings. However, gonioscopic examination usually identifies the inferior quadrant as the widest in gonioscopy. In contrast, our UBM suggested it to be narrower than nasal and temporal quadrants.

Linear regression model suggested that the angle width and recess area (AOD250, AOD500, ARA) were not linearly associated with age ($P>0.05$). They were narrower in women than men (ß=-0.04 for AOD250, ß=-0.067 for AOD500, ß=-0.063 for ARA, $P<0.001$ for all). The proportion of variation of UBM measurements explained by variation in age and gender (R^2) in linear regression model was found to be 12.3% for AOD250, 19.3% for AOD500 and 35.5% for ARA.

3.3.3.2 Iris thickness in normal subjects

The iris thickness 750 microns from the scleral spur (IT750) was similar in all 4 quadrants, while iris thickness at 1000 microns (IT 1000) tended to be thicker in nasal and inferior quadrants (ANOVA, $p<0.05$). Mean IT750 ranged from 0.445mm to 0.451mm in 4 quadrants, while mean IT1000 ranged 0.475mm to 0.493mm. Median iris curvature was found to be steepest in the superior quadrant followed by nasal, and least in temporal and inferior quadrants (ANOVA, $P<0.05$). This pattern was in consistent with the degree of angle width (AOD) suggested by UBM (**Table 41**).

The iris thickness at 750 microns was thinner in women than men (ß=-0.036,

P=0.031) but was not significantly associated with age (R^2=7%, P=0.09). No linear association of IT1000 with age or gender was found (F test, P=0.867).

Linear associations between UBM measurements were also investigated. No linear association was found between AOD and iris thickness either at 750 or 1000 microns locations (F test, P>0.05), suggesting this is no inevitable relationship between angle width and peripheral iris thickness. A positive linear association was found between AOD and TCPD (R^2=37%, P<0.0001). In subjects with normal, open angles the space occupied by the peripheral iris accounts for only a small proportion of the total distance. Angle width (AOD250, AOD500 and ARA) tended to be narrower if the iris insertion was more anteriorly positioned (scleral spur to iris insertion distance, SS-IR, smaller) (linear regression model for ARA, ß=0.56, P<0.0001, R^2=39%). The AOD500 decreased by 1 mm if the iris insertion was 0.6mm anterior located (ß=0.59, R^2=21%, P<0.0001). The association of AOD with iris thickness differed in the narrow angle group (described in the followed section).

3.3.4 UBM quantitative characteristics in narrow angle eyes

Association of UBM quantitative parameters were also investigated in the narrow angle subjects (**Table 39**). Mean AOD250 and AOD 500 in normal, control subjects were 0.090mm and 0.152mm respectively. In people with narrow angles, the AOD250 was approximately half this value (mean: 0.047,SD: 0.038mm, P<0.0001, unpaired t test), whereas the AOD500 was about one third of the value seen in normal control subjects (0.054mm, P<0.0001, t test). The ARA in narrow angle eyes were also significantly smaller than in normal controls (normal 0.105 sq mm, narrow 0.044 sq mm, P<0.0001, t test) and the iris insertion tended to more anteriorly-located relative to the scleral spur in narrow angle eyes (normal 0.120mm; narrow 0.101mm), although this was of marginal significance(P=0.059, t test).

The association between UBM parameters and the Shaffer grades of drainage angle width derived from gonioscopic assessment were examined (**Table 42, Table 39**). A positive association between the angle width related parameters (AOD250, AOD500, ARA750) and gonioscopic Shaffer angle width was

identified in this group of subjects. However, the association between iris insertion and Shaffer angle width was not consistent. The more convex the iris (smaller radius of curvature), the narrower the gonioscopic angle width was.

3.3.5 UBM qualitative characteristics in narrow angle eyes

Table 43 presents the qualitative descriptions of the superior quadrant of right eyes in case and control groups (all images were taken in dark room). Except for there being more medium and thick basal iris in the Case group, other qualitative characteristics in case and control groups were not significant different in the superior quadrant.

3.3.6 UBM appositional closure

In UBM images, some degree of appositional closure (**Figure 19**) was identified in 79% of narrow angle subjects and 44% of normal control subjects in the superior quadrant. Similarly, these proportions were 40% and 16% nasal, 60% and 29% inferior, 26% and 14% in temporal quadrants (**Table 44**). One reason that appositional closure was seen in normal control subjects was because of the selection criteria: control subjects were identified according to the amount of posterior, pigmented TM that could be seen. If this was visible in less than two complete quadrants were classified as "narrow". If not, they were eligible as "controls". Furthermore, the lighting and inevitable indentation resulting from gonioscopy artificially open the drainage angle may also be in part responsible for some of the discrepancy between UBM and gonioscopic classification.

It has been proposed that the natural history and clinical characteristics of angle-closure may be more clearly understood by identifying the level at which closure occurs. Two categories are described: In "B type", closure starts at the periphery of the drainage angle. In "S type" closure, the process involves initial contact between iris and the corneo-scleral coat at or near the level of Schwalbe's line (**Figure 19** in method section). Posterior to this contact lies an aqueous filled space first hypothesized by Mapstone, and later proven on UBM examination by Ritch's group (**Figure 19** in method section). In the cases with

pigmented TM not visible in at least 2 quadrants, appositional closure confirmed by UBM in the dark was observed in 79% in superior quadrants, these proportions decreased in inferior quadrant (60%), nasal (40%) and temporal (26%). The same pattern was observed in the control group, decreasing from superior (44%), to inferior (29%), nasal (16%) and temporal (26%). Among narrow angle subjects with some degree of appositional closure, "B-type" closure was observed roughly in 1/3 of them (**Table 44**). Among normal controls who had some identifiable appositional contact, again about a third of cases had "B-type" configuration., with the exception of the inferior angle, in which this phenomenon was only seen in 5% of subjects. In the analysis of the characteristics of cases with appositional closure, all cases with established PAS (PAC or PACG cases) were excluded.

3.4 Changes following laser iridotomy

There were a total of 140 subjects with occludable angles in either eye who were offered laser iridotomy. About half of them (74 subjects) accepted the offer of laser treatment within this phase of the study. The participation rate was around 60% in those in 50-59, 60-69 and 70+ years of age (the highest was in 50-59 years). Only 10% of the 20 subjects in 9th decade accepted treatment. The demographic characteristics of those who attended and did not attend were not statistically significant after excluding those aged 80+ years. All the subjects who agreed to participate in the study also took part in the UBM examination at baseline. Of the subjects with narrow angles who agreed to participate in the UBM examination, 85% (74/84) subsequently underwent laser PI.

The iridotomy was patent in all but one eye after a single treatment session. Patency was ascertained by slit lamp examination and UBM imaging. The size of the iridotomy was approximately 0.2-0.3 mm in all cases. The one case in which the iridotomy was not fully patent underwent repeat UBM examination after successful iridotomy was completed. Two weeks after the laser procedure, patients returned for a follow-up examination (**Table 45-46**). The mean IOP before LPI treatment (14.3 mm Hg, 95% CI: 13.6~15.0) was close to the population mean in 1,405 subjects (15.2 mm Hg, 95% CI:14.9~15.3). After LPI, the IOP decreased by an average of 3 mmHg (Paired t test, $P<0.0001$). The

mean axial ACD measured by optical pachymetry did not change significantly after LPI, with a mean of 2.04 mm before and after (Paired t test, P=0.806). Other biometric parameters, lens thickness, axial length, did not change significantly after LPI. However, the Shaffer angle width increased significantly in both superior and inferior quadrants, the mean of Shaffer units increased by 300% times, from 0.6 units before LPI to 2.4 units after LPI.

The apparent iris insertion before and after LPI, based on Spaeth's gonioscopic grading system is shown in **Table 47**. After the LPI procedure, the proportion of Grade A or B dropped from 97% to 61% in the superior quadrant, from 73% to 28% nasally, from 56% to 17% in the inferior quadrant and from 85% to 22% temporally. Except for the superior quadrant, over 80% of eyes with an apparent iris insertion Grade A to B before iridotomy were converted to Grade C or D after the LPI procedure.

From a total of 74 eyes receiving LPI, about one-fifth (14/74) of eyes remained "occludable" after treatment (i.e. the posterior, usually pigmented, TM could not be seen in 3 or more quadrants). Those in whom the angle remained occludable after LPI tended to be younger and male, although this trend was not statistically significant. Regarding the gonioscopic iris profile after laser PI, the eyes with angles that remained occludable had a higher rate of plateau iris (92.3%, Chi-square, P<0.0001) compared to the eyes that were opened following PI (26.4%). The ACD measured by optical pachymetry was not statistically different (2.03 mm in eyes with open angles versus 2.08 mm in those remaining closed, P=0.325). Limbus ACDs were graded as 5% of CT in 6 eyes (42.9%) and 15% in 8 eyes (57.1%) in the angles remaining occludable following PI, however, these grades were 5% in 28 eyes (49.1%), 15% in 16 (28.1%), 25% in 19.3%, 40% or more in 2 eyes (3.5%) in the angles opened after treatment at the baseline. The LCD gradings in these two groups were not statistically sigifnicant (Chi Square test, P=0.192).

UBM data was available for 72 out of 74 eyes that had undergone laser PI procedure. **Table 48** summarizes the number of quadrants with UBM evidence of appositional closure before and after laser PI. Before this treatment, 95% of eyes (68/72) had appositional closure in at least one quadrant. This proportion

was reduced to 59% (42/72) after laser PI. There were variations between quadrants in the changes in proportions with appositional closure. About half of all cases with appositional closure in the superior quadrant reversed following laser PI (30/63), but these proportions were much higher in other quadrants: 63% (24/38) nasally, 48% (26/54) inferiorly and 78% (14/18) in the temporal quadrant. **Table 49** summarizes the changes in UBM angle width parameters (AOD250, AOD500, ARA750, area ratio of iris versus angle) before and after laser PI procedure. After laser PI, the means of all these parameters increased very significantly. The percentage increase in all 4 quadrants in AOD250, ranged from 30% temporally to 57% in the superior quadrant. However, considering AOD500, there was a dramatic increase in the width of the superior quadrant (156%), while the other 3 quadrants increased by between 50% (nasally) and 60% (temporal and inferior quadrants). A similar trend in increase was seen in ARA 750. A 75% increase in the means occurred in all 4 quadrants. The area ratio of iris to peripheral drainage angle showed a marginal decrease, from 71% to 69% (P= 0.076). Thus, these UBM data document an increase in angle width after iridotomy in the eyes of people in Southern China

When compared with the change in mean AOD250 in the four quadrants, among the 73 eyes with laser PI treatment and available UBM data, 54 (74%) eyes had an increase on the AOD250, leaving 19 eyes (26%) with an AOD unchanged or reduced after laser PI. The proportions for AOD500 were 88% (increasing) and 12% (no change or decline). **Figure 40** and **Figure 41** are scatter plots showing the AOD250 and AOD500 before and after laser PI. It can be seen that most of the eyes with no change or a decrease in AOD250 were at the lower end of the angle width, perhaps suggesting either crowding of the angle by the peripheral iris, or simply that the accuracy and precision of measurement in eyes with very small AOD was limited.

It appears that the structure of the iris and ciliary body, in part, determine the potential change in the drainage angle after laser PI. **Table 50** summarizes these changes after laser PI. The radius of curvature of the posterior surface of the iris increased from 5.02 to 13.31 mm indicating a flattening of iris contour after iridotomy. There was significant amount of flattening in all 4 quadrants ($P<0.0001$). The distance between TM and ciliary body (TCPD) also increased

significantly from 0.537 mm to 0.561 mm (4.5%, P<0.0001) suggesting the ciliary body moving backward after the treatment. It is also interesting, but not surprising, to find the distance between back of iris and the ciliary body (ICPD) decreased after the treatment (**Figure 42**) that may be attributable to flattening of the peripheral iris which takes the iris closer to the ciliary body. Iris thickness at both 750 and 1000 microns from the scleral spur increased after the treatment suggesting that when pupil block is eliminated, the iris becomes flattened and is presumably under less tension, and therefore the thickness increases.

Table 51 summarizes the qualitative changes after laser PI. There were no eyes with a "moderate" or "extreme" iris convexity after laser PI. A marked decrease was also seen in the proportion of irises with a pronounced angulation in the peripheral third. This decreased from 11% to only 1.4%. It is interesting to find the proportion of eyes with a ciliary body graded as anteriorly rotated increased by 5% after laser PI.

Table 52 shows the UBM parameters in those eyes whose angles remained closed gonioscopically after laser PI. They tended to have smaller AODs measured at 250 (0.071 mm vs. 0.049 mm, P=0.09) and 500 microns (0.108 mm vs. 0.052 mm, P=0.001) from the scleral spur, compared with those that were open after laser PI. Furthermore, the iris insertion tended to be more anterior; the distance from the iris insertion to the scleral spur was 1/3 closer to the scleral spur (P=0.061). The iris tended to be thicker at both 500 and 1000 microns from the scleral spur (at 500 microns for angles being opened by laser PI versus not: 0.376mm vs 0.399mm, P=0.095; at 1000 microns: 0.415mm vs 0.447mm, P=0.041). The ciliary body was more anteriorly rotated (smaller distance between scleral spur and ciliary body) in the eyes remaining occludable (0.562mm vs 0.514mm, P=0.033). However, the distance between back of the iris to ciliary body was not significantly different in these two groups (0.078mm vs 0.075mm, P=0.781).

Figures 43-45 demonstrates the typical changes in angle configuration following PI. **Figures 46-53** show typical UBM characteristics in eyes in which the angles did not open following treatment.

As expected, a common observation in eyes after laser PI is a flattening of the posterior surface of the iris. This can be seen in eyes with both angles that that opened an those that remained closed. The characteristics of angles that opened after laser PI included:

1. Thin iris (**Figure 44**): when the iris was judged to be thin, particularly in basal peripheral area, the angles often open after PI. The characteristics of iris insertion and anterior rotation of the ciliary body were not determining factors if the iris was thin.
2. Neutral ciliary body: When the ciliary body was in a neutral position (not anteriorly rotated) and the iris insertion was not anteriorly-located, or peripheral iris was not particularly thick, the angle usually opened after laser PI (**Figure 45**).
3. Posterior iris insertion: when the iris insertion was posterior, into the middle or apex of the ciliary body, angles tended to open after laser iridotomy, as long as the peripheral iris was not very thick, regardless of the presence of ciliary body rotation.

When PAS were present, it appeared that laser PI was unlikely to open the angle in all cases (at least within 2 weeks of treatment) (**Figure 46**). Iridotomy was found not to be patent in one case. A second laser PI had to be performed in only one case. (**Figure 47**)

The following UBM features are typical for the angles that do not open after the laser PI.

1. Anterior rotation of the ciliary body: this was a prominent feature in most angles that did not open after PI(**Figure 48**). An anteriorly-rotated ciliary body supports the back surface of the iris and prevents backward movement of the iris. Before laser PI, relative anterior rotation of the ciliary body may exist but there is often separation between the posterior surface of the iris and ciliary body disguising this. After laser PI, with flattening of the iris profile, the effect of anterior rotation of the ciliary body is revealed. In the presence of a thick iris this effect will be further exaggerated (**Figure 49**).
2. Angulated iris insertion (**Figure 50, 53**): After laser PI, the peripheral iris remained angulated to some extent in eyes with residual angle-closure,

contributing to narrowing of the drainage angle, even when neither ciliary body rotation nor a thick peripheral iris thickening were present.

3. Anterior insertion of the iris (**Figure 51**): When anterior rotation of ciliary body exists, the space between the ciliary body and the TM is limited. In this scenario, a thick iris will occupy a greater proportion of the available space. When the iris insertion is anterior, the space between the anterior surface of the iris and TM is further limited, and therefore, angle width may not change as greatly as in eyes with a more posterior iris insertion.
4. Thick peripheral iris (**Figure 52**): Thick peripheral iris will occupy a greater proportion of the space adjacent to the drainage angle. Even when the ciliary body is not anteriorly-rotated, and the space between ciliary process and TM is large, a thick iris can still cause narrowing of the angle.

Table 6 Demographic comparison of sample, sampling frame and target population *

Population	Enumerated sample (%) ‡			Sampling frame (%)**			District (%)		
Age	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
50-59	430	403	833	2578	2299	4877	22310	20484	42794
	(39.0)	(33.3)	(36.0)	(39.5)	(30.1)	(35.0)	(39.0)	(32.6)	(35.7)
60-69	301	332	633	2071	2581	4652	19138	22910	42028
	(27.3)	(27.4)	(27.4)	(31.8)	(34.8)	(33.3)	(33.4)	(36.4)	(35.0)
70-79	271	340	611	1443	1821	3264	12518	14200	26718
	(24.6)	(28.1)	(26.4)	(22.1)	(24.5)	(23.4)	(21.9)	(22.6)	(22.3)
80+	101	135	236	430	719	1149	3176	5268	8444
	(9.2)	(11.2)	(10.2)	(6.6)	(9.7)	(8.2)	(5.5)	(8.4)	(7.0)
Total	1103	1210	2313	6522	7420	13942	57142	62862	120004
	(47.7)	(52.3)	(100)	(46.8)	(53.2)	(100)	(47.6)	(52.4)	(100)

Percentages given in brackets represent age- and sex-specific sub-totals

** This data was derived from National Census 2000 and obtained with approval from the Guangzhou City Government: Bureau of Statistics. The sample was drawn in September 2003, the Census data was collected in 2000.

** *Fengyuan* street was selected from 12 street blocks in the district. This was considered the sample frame.

‡ The sample was drawn from 2 out of 10 primary sample units (clusters) selected at random in the *Fengyuan* street block.

Table 7 Demographic characteristics of subjects selected and examined

Age	50-59		60-69		70-79		80-93		Total
Sex	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	**Men**	**Women**	
Died **	1	3	1	1	4	2	4	3	19
Moved from area **	97	78	65	53	48	40	18	31	430
Refused examination	38	37	22	23	14	15	7	12	168
Severely ill	2	3	2	7	7	16	14	15	66
Did not attend‡	81	18	35	21	18	28	11	13	226
Examined, home & clinic	211	264	175	228	180	239	47	61	1405
% Eligible subjects examined	63.6	82.0	74.8	81.7	82.2	80.2	59.5	60.4	75.3
Sub-total for sex	430	403	300	333	271	340	101	135	2313
Total for age	**833 (36.0)**		**633 (27.4)**		**611 (26.4)**		**236 (10.2)**		**2313 (100)**

** Considered not eligible for the examination, ‡ Includes those who occupied the enumerated household but not contactable in 3 visits and those who agreed at the door to door enumeration but did not attend the examination.

Table 8 – Vertical cup to disc ratio in normal subjects*

	Right CDR (95% *CI*‡)	Left CDR (95% *CI*‡)	Asymmetry ** (95% *CI*‡)
N (CDR measurements)	1271	1263	1240
0.5th Percentile	0.1 (0, 0.2)	0.1 (0, 0.2)	0 (0, 0)
2.5th Percentile	0.2 (0.2, 0.2)	0.2 (0.2, 0.2)	0 (0, 0)
Median	0.4 (0.4, 0.4)	0.4 (0.4, 0.4)	0 (0, 0)
97.5th Percentile	0.7 (0.7, 0.8)	0.7 (0.7, 0.8)	0.2 (0.2, 0.2)
99.5th Percentile	0.8 (0.8, 0.9)	0.8 (0.8, 0.9)	0.3 (0.3, 0.4)

* Defined as those with available VCDR data and excluding eyes with definitive glaucomatous field defect (46 right, 48 left)
** Asymmetry was defined as the absolute value of the difference on VCDR in two eyes
‡ Calculated based on binomial contribution assumption

Table 9 – Intraocular pressure in normal subjects (mmHg)* (Tonopen tonometer)

	Right IOP (mmHg)	Left IOP (mmHg)
N (IOP measurements)	1326	1325
0.5th Percentile	7 (6, 8)	8 (6.5, 8.7)
2.5th Percentile	10 (9, 10)	10 (9,10)
Median	15 (15, 15)	15 (15,15)
Mean (SD)	15.2 (3.07)	15.1 (3.25)
97.5th Percentile	21 (21, 22)	21 (21, 22)
99.5th Percentile‡	24.0 (24, 28)	24.3 (23, 28)

* IOP was measured by Tono-pen tonometer after excluding eyes with definitive glaucomatous field defect.
‡ Corresponds to the cut-off selected for category 3 in diagnostic criteria for glaucoma.

Table 10-Prevalence of all glaucoma by age and sex

	Men	Diagnostic category				Women	Diagnostic category				Total	
	N	1	2	3	Prevalence (95% CI)	N	1	2	3	Prevalence (95%CI)	N	Prevalence (95%CI)
50 to 59	211	3	1	0	1.9 (0.4, 3.7)	264	1	0	0	0.4 (0.4, 1.1)	475	1.1 (0.1, 2.0)
60 to 69	175	6	2	0	4.6 (1.4, 7.7)	228	2	2	0	1.8 (0.3, 3.5)	403	2.9 (1.3, 4.6)
70 to 79	180	5	3	2	5.6 (2.2, 8.9)	239	7	3	3	5.4 (2.5, 8.3)	419	5.5 (3.3, 7.6)
80 to 93	47	3	5	2	21.3 (9.1, 33.4)	61	1	1	1	4.9 (0.0, 10.5)	108	12.0 (5.8, 18.3)
All	613	17	11	4	5.2 (0.3, 7.0)	792	11	6	4	2.6 (1.5, 3.8)	1405	3.8 (2.8, 4.8)

Table 11 Mechanism and characteristics of glaucoma

Diagnosis	Sex ratio (M:F)	Median age (range)	Diagnostic category			Blind* in at least one eye (% of total)	Previously diagnosed (%)
			1	2	3		
POAG	21:8	72 (53, 89)	20	8	1	5 (17.2)	2 (6.9)
PACG‡	8:13	74 (61, 90)	8	7	6	9 (42.9)	12 (57.1)
Secondary	2:0	54, 88	0	1	1	1 (50.0)	0 (0.0)
Others **	1:0	80	0	1	0	1(100)	0
Total	32: 21	73 (53, 90)	28	17	8	16 (30.2)	14 (26.4)

* Defined as best-corrected visual acuity 3/60 or worse.

** Mechanism is not determined: both eyes had undergone cataract surgery with diffuse board PAS, angle status before surgery is not determinable.

‡ Eight cases (38%) had previous acute angle-closure attack.

Table 12 List of the characteristics of definitive glaucoma cases

ID	Age	Sex	Side	History*	Presenting VA**	IOP (mmHg)	Occludable angle‡	PAS §	VCDR	Field ※	Diagnosis	Category	Comment
2-2-7-1	74	F	OD	No	20/40	16	N	N	0.6	R-G	POAG	1	
			OS	No	20/32	17	N	N	0.7	R-G	POAG	1	
2-3-40-1	80	F	OD	No	20/40	16	N	N	0.7	Mis	DS		
			OS		20/40	17	N	N	0.9	Mis	POAG	2	
2-5-17-1	58	M	OD	No	20/200	18	N	N	0.6	N-G	Normal		
			OS	No	20/100	18	N	N	1.0	R-G	POAG	1	
2-6-12-1	73	M	OD	No	20/25	18	N	N	0.9	R-G	POAG	1	
			OS	No	20/32	13	N	N	0.7	N-G	DS		
2-7-11-1	76	F	OD	No	20/80	21	Y	N	0.7	R-G	DS		
			OS	No	20/40	21	Y	N	0.9	R-G	PACG	1	
2-7-16-1	82	M	OD	No	20/80	12	N	N	0.9	Miss	POAG	2	CHECK
			OS	No	20/80	11	N	N	0.8	Miss	POAG	2	
2-7-20-1	62	M	OD	No	20/40	15	N	N	0.7	N	DS		
			OS	No	20/25	14	N	N	0.9	R-G	POAG	1	
2-7-21-1	76	F	OD	No	20/800	16	N	Y	0.9	R-G	POAG	1	High myopia
			OS	No	20/200	16	N	Y	0.7	R-G	POAG	1	High myopia
2-7-34-1	78	F	OD	Trab	HM	16	Y	Y	1.0	Miss	PACG	3	
			OS	PI	20/400	18	N	N	0.9	R-G	PACG	1	
2-7-40-2	67	F	OD	No	20/32	19	Y	N	0.7	Miss	PACG	2	
			OS	No	20/32	20	Y	N	0.4	Miss	Normal		
2-8-39-1	55	F	OD	N	20/125	14	N	N	0.8	R-G	POAG	1	
			OS	N	20/80	14	N	N	0.7	R-G	POAG	1	
2-8-44-1	67	M	OD	N	20/32	14	N	N	1.0	R-G	POAG	1	
			OS	N	20/32	17	N	N	0.8	R-G	POAG	1	
2-8-57-1	80	F	OD	N	20/40	14	Y	N	0.9	R-G	POAG	1	
			OS	N	20/40	13	Y	N	0.8	R-G	POAG	1	
2-8-63-1	78	F	OD	Trab	NLP	21	Y	Y	Miss	Miss	PACG	3	Cataract
			OS	PI	20/163	10	Y	Y	0.7	Miss	PACS		

2-9-9-1	69	M	OD	N	20/32	19	N	N	0.7	N	DS		
			OS	N	20/25	19	N	N	0.9	R-G	POAG	1	
2-10-24-1	64	M	OD	N	20/32	17	N	N	0.6	N	Normal		
			OS	N	20/40	15	N	N	0.7	R-G	POAG	1	
2-10-93-1	53	M	OD	N	20/100	17	N	N	0.8	R-G	POAG	1	
			OS	N	20/160	15	N	N	0.7	R-G	POAG	1	
2-10-94-1	89	M	OD	N	20/80	19	N	N	0.8	Miss	DS		
			OS	N	20/80	19	Y	N	0.8	R-G	POAG	1	Mixed mech
1-11-12-1	70	M	OD	N	20/32	20	N	N	0.8	R-G	POAG	1	
			OS	N	20/160	25	N	N	0.9	R-G	POAG	1	
1-11-20-1	73	F	OD	N	20/200	12	N	N	0.9	R-G	POAG	1	
			OS	N	HM	15	N	N	Miss	Miss			Mature cat.
2-12-4-1	53	M	OD	N	20/25	16	N	N	0.8	R-G	POAG	1	
			OS	N	20/32	16	N	N	0.6	S-G			
1-12-8-1	86	F	OD	PI	20/125	18	Y	Y	Miss	Miss	PACG	3	
			OS	Trab	20/252	18	Y	Y	Miss	Miss	PACG	3	
1-12-26-1	78	F	OD	N	20/32	26	Y	Y	0.8	R-G	PACG	1	
			OS	N	20/32	22	Y	Y	0.7	R-G	PACG	1	
1-12-30-1	75	F	OD	N	20/80	17	Y	N	0.7	--	PACG	2	Check
			OS	N	20/32	18	Y	N	0.4	--	PACS		
1-12-40-2	89	M	OD	N	FC	9	N	N	1.0	Miss	POAG	2	
			OS	N	20/40	11	N	N	0.8	R-G	POAG	1	
1-14-60-1	72	M	OD	N	20/50	16	N	Y	0.7	N			
			OS	N	20/50	22	Y	Y	1.0	U-G	PACG	2	
1-16-52-1	80	M	OD	N	20/40	10	N	N	0.9	R-G	POAG	1	
			OS	N	20/40	12	N	N	0.5	N	Normal		
1-16-68-2	63	M	OD	N	20/160	18	N	N	0.9	U-G	POAG	2	
			OS	N	20/63	16	N	N	0.9	U-G	POAG	2	
1-16-87-2	74	F	OD	Episode	20/200	22	Y	Y	0.9	R-G	PACG	2	
			OS	Episode	20/100	18	Y	Y	0.8	R-G	PACG	2	
16-103-01	67	F	OD	N	20/32	16	Y	N	0.5	U-G	PACS		
			OS	Episode	20/125	16	Y	N	0.8	R-G	PACG	1	
16-140-1	71	F	OD	N	20/40	26	Y	N	0.4	Miss	PACS		

			OS	TRAB+IOL	20/32	22	Y	N	0.7	Miss	PACG	2	
16-143-2	76	M	OD	Episode	HM	18	Y	Y	Miss	Miss	PACG	3	
			OS	Episode	20/80	20	Y	Y	0.9	Miss	PACG	2	
16-149-1	90	M	OD	TRAB	NLP	Miss	Miss	Miss	Miss	Miss	PACG	3	Home visit
			OS	TRAB	NLP	Miss	Miss	Miss	Miss	Miss	PACG	3	Home visit
1-20-1-1	80	M	OD	N	20/32	11	N	Y	0.8	Miss	POAG	2	Check
			OS	N	20/32	12	N	Y	0.8	Miss	POAG	2	
1-21-8-1	88	M	OD	N	20/50	17	N	N	0.3	Miss	Normal		
			OS	N	HM	55	Y	Y	Miss	Miss	SeG	3	
1-21-11-2	62	M	OD	Episode	20/25	30	Y	Y	1.0	R-G	PACG	1	
			OS	Phaco	HM	43	Y	Y	0.5	R-G	PACG	1	
1-21-18-2	83	M	OD	N	20/80	13	N	N	0.9	Miss	POAG	2	CHECK
			OS	N	20/160	15	N	N	0.9	Miss	POAG	2	
1-23-3-2	61	F	OD	Episode+PI	20/32	26	Y	Y	0.8	R-G	PACG	1	
			OS	Episode+PI	20/40	19	Y	Y	0.9	R-G	PACG	1	
1-24-44-1	74	F	OD	N	20/40	17	Y	N	0.6	U-G			
			OS	N	20/63	20	Y	Y	0.7	R-G	PACG	1	
1-25-28-1	70	F	OD	Trab	20/80	14	Y	Y	0.9	R-G	PACG		CHECK
			OS		20/320	15	N	Y	0.5				
2-27-8-1	62	M	OD		20/32	21	N	N	0.8	R-G	POAG	1	
			OS		20/32	17	N	N	0.6	N			
1-30-77-1	78	F	OD		20/32	27	N	Y	0.4	N			CHECK
			OS		20/100	22	Y	Y	1.0	R-G	PACG	1	
2-34-4-1	80	M	OD		20/63	14	N	N	0.9	R-G	POAG	1	
			OS		20/50	15	N	N	0.9	R-G	POAG	1	
2-35-24-2	67	F	OD		20/25	17	N	N	0.7	R-G	POAG	1	
			OS		20/32	19	N	N	0.8	R-G	POAG	1	
2-35-42-1	74	F	OD		20/200	19	N	N	0.8	N-G			
			OS		20/63	20	N	N	0.9	R-G	POAG	1	
2-35-47-2	87	M	OD		20/125	15	N	N	1.0	R-G	POAG	1	
			OS		20/63	15	N	N	1.0	R-G	POAG	1	
2-36-15-1	73	F	OD	Trab	20/100	16	Y	Y	Miss	Miss	PACG	3	Check
			OS	Trab	20/80	14	Y	Y	Miss	Miss	PACG	3	

2-36-15-2	77	M	OD		20/50	13	N	N	0.9	R-G	POAG	1	
			OS		20/50	13	N	N	1.0	R-G	POAG	1	
2-36-22-1	72	M	OD	N	20/40	13	N	N	0.9	U-G	POAG	2	
			OS	N	20/40	14	N	N	0.7	U-G			
2-36-26-2	73	M	OD	Episode+trab	20/80	11	Y	Y	0.9	R-G	PACG	1	
			OS	Episode+PI	20/40	10	N	Y	0.6	N-G			PAC
2-39-2-2	54	M	OD	N	20/800	24	NY	Y	0.8	Miss	SeG	2	Traumatic
			OS	N	20/32	11	N	N	0.4	Miss			
2-40-6-1	67	M	OD	Trab	HM	14	Y	Y	1.0	Miss	PACG	2	
			OS		20/63	12	N	N	0.5	Miss			
2-40-35-1	75	M	OD		20/640	18	N	N	0.8	Miss	POAG	2	BRVO
			OS		20/40	16	N	N	0.7	Miss	DS		

* Trab: Trabeculectomy; N: No glaucoma-related history; Episode: previous history on acute episode; PI: peripheral iridectomy or laser iridotomy; IOL: intraocular lens; Phaco: phacoemulsification procedure.

** NLP: no light perception; FC: finger counting; HM: hand movements

‡ Occludable angle is defined as the pigmented trabecular meshwork not being visible for 270 degrees or more of the angle circumference. Miss: missing data.

§ PAS: any recorded peripheral anterior synechiae by gonioscopy examination.

※ R-G: repeatable glaucomatous field defect; U-G: glaucomatous field defect, not repeated; N-G: visual field defect but not compatible to glaucoma; N: normal visual field; Miss: missing field data.

Table 13 Prevalence of occludable angle, primary angle closure, primary angle closure glaucoma*

Men	N **	All occludable angles	Primary angle closure	Primary angle closure glaucoma‡
50 to 59	206	1.9 (0.4~3.8)	0 (0~0)	0
60 to 69	172	8.7 (4.5~13.0)	1.7 (0~3.6)	1.1
70 to 79	172	10.5 (5.8~15.1)	1.7 (0~3.6)	2.8
80 to 93	41	12.2 (1.7~22.7)	2.1 (0~6.4)	2.1
All	591	7.1 (5.0~9.2)	1.1 (0.3~2.0)	1.3 (0.4~2.2)
Women				
50 to 59	260	5.0 (2.3~7.7)	1.9 (0.2~3.5)	0
60 to 69	226	13.7 (9.2~18.2)	3.9 (1.4~6.5)	1.3
70 to 79	236	16.5 (11.8~21.3)	3.7 (1.4~6.2)	3.7
80 to 93	59	25.4 (14.0~36.9)	4.9 (0~10.5)	1.6
All	781	12.5 (10.2~14.9)	3.3 (2.0~4.5)	1.6 (0.7~2.5)
Men and women				
50 to 59	466	3.7 (1.9~5.4)	1.1 (0.1~2.0)	0
60 to 69	398	11.6 (8.4~14.7)	2.9 (1.3~4.6)	1.2
70 to 79	408	14.0 (10.6~17.3)	2.9 (1.3~4.5)	3.3
80 to 93	100	20.0 (12.0~28.0)	3.7 (0.8~7.3)	1.9
All	1372	10.2 (8.6~11.8)	2.4 (1.6~3.1)	1.5 (0.9~2.1)

* The prevalence is based on the individual (either eye of the individual); the diagnosis is made when the particular characteristic is identified in either eye. The diagnosis is made according to the eye with more severe form if the disease status is different in two eyes. For example, when the case presented with suspect angle closure in one eye and with PAC in the other eye, a diagnosis of PAC, instead of angle closure suspect, is made. Prevalence rate for primary angle-closure suspects refers to all occludable angles found by gonioscopy (including PACG and PACG).
** The cases with missing data in gonioscopy are not included.

Table 14 – Cause of blindness based on best corrected visual acuity*

	One or both eyes	Both eyes
Cataract	31 (43.3)	1
Glaucoma	10 (14.9)	1
AMD	4 (6.0)	
Vascular retinal disease	4 (6.0)	
High myopia retinopathy	4 (6.0)	1
Pigmentary retinopathy	3 (4.5)	2
Trauma	2 (3.0)	
Diabetic retinopathy	2 (3.0)	1
Corneal	1 (1.5)	
Others**	8 (11.9)	
Total	71	6
Prevalence (%) **	5.1	0.4
95% CI of prevalence	3.9~6.2	0.1~0.8

* Based on best corrected visual acuity < 3/60 with subjectively-refined refractive correction or constriction of visual fields to less than 5 degrees from fixation.

** Others included: Retinal detachment (1), uncorrected aphakia(1), pthisis/disorganized(1), amblyopia(1), optic atrophy(1), undetermined (3).

AMD: age-related macular degeneration

Table 15 – Cause of blindness based on presenting visual acuity*

	One or both eyes	Both eyes
Cataract	31(38.3)	2
Glaucoma	15 (17.4)	1
Uncorrected refractive error	6 (6.9)	1
High myopia retinopathy	4 (4.7)	
AMD	4 (4.7)	
Vascular retinal disease	4 (4.7)	
Pigmentary retinopathy	3 (3.5)	2
Diabetic retinopathy	2 (2.3)	1
Corneal	2 (2.3)	
Amblyopia	3 (3.5)	
Cataract complications	4 (4.7)	
Optic atrophy	2 (2.3)	
Others §	4 (4.7)	
Total	86 (100)	7
Prevalence (%) **	6.1	0.5
95% CI of prevalence	4.9~7.4	0.1~0.9

* Based on presenting visual acuity (with correction if worn) < 3/60 and severe visual field constriction to less than 5 degree.

§ Others included: corneal transplantation(1), retinal detachment(1), trauma(2), undertermined(1), pthisis(1), cataract complication(1-corneal decompensation, 1-PCO).

AMD: age-related macular degeneration

Table 16- Intraocular pressure in all subjects (Tono-pen tonometer- right eyes) *

Men	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	210	15.2 (14.8, 15.6)	2.9	5, 24	13	15	17	1
60 to 69	173	15.1 (14.6, 15.7)	3.7	8, 30	12	15	17	2
70 to 79	173	14.9 (14.4, 15.3)	2.9	7, 24	13	15	17	7
80 to 93	41	13.7 (12.8, 14.6)	2.9	8, 19	11	14	16	6
All	597	15.0 (14.7, 15.3)	3.2	5, 30	13	15	17	16
Women	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	263	15.5 (15.1, 15.8)	2.8	7, 24	14	16	17	1
60 to 69	225	15.6 (15.2, 16.1)	3.3	7, 29	14	16	17	3
70 to 79	236	15.2 (14.8, 15.6)	3.1	8, 27	13	15	17	3
80 to 93	57	14.7 (13.8, 15.6)	3.4	6, 28	13	15	16	4
All	781	15.4 (15.2, 15.6)	3.1	6, 29	13	16	17	11
Men and women	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	473	15.4 (15.1, 15.6)	2.9	5, 24	13	15	17	2
60 to 69	398	15.4 (15.1,15.8)	3.5	7, 30	13	15	17	5
70 to 79	409	15.1 (14.8, 15.4)	3.0	7, 27	13	15	17	10
80 to 93	98	14.3 (13.6, 14.9)	3.2	6, 28	12	14	16	10
All	1378	15.2 (15.1, 15.4)	3.1	5, 30	13	15	17	27

* Missing data in 27 right eyes are not included. Missing data in cases with corneal diseases or in subjects who could not co-operate.

Table 17- Axial anterior chamber depth in phakic subjects (optical pachymetry- right eyes) *

Men	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	193	2.72 (2.67, 2.76)	0.31	1.94, 3.82	2.53	2.71	2.90	17
60 to 69	162	2.58 (2.52, 2.63)	0.37	1.27, 3.88	2.33	2.60	2.83	8
70 to 79	154	2.49 (2.43, 2.54)	0.34	1.49, 3.36	2.24	2.49	2.72	19
80 to 93	32	2.43 (2.30, 2.57)	0.38	1.44, 3.12	2.28	2.50	2.68	9
All	541	2.59 (2.56, 2.62)	0.36	1.27, 3.88	2.37	2.61	2.82	53
Women	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	247	2.53 (2.49, 2.57)	0.30	1.75, 3.31	2.30	2.50	2.73	15
60 to 69	213	2.39 (2.35, 2.43)	0.29	1.32, 3.26	2.21	2.38	2.60	11
70 to 79	200	2.34 (2.29, 2.38)	0.33	1.29, 3.26	2.11	2.35	2.52	19
80 to 93	47	2.27 (2.19, 2.34)	0.26	1.74, 2.76	2.05	2.29	2.46	12
All	707	2.42 (2.39, 2.44)	0.32	1.29, 3.31	2.21	2.41	2.63	57
Men and women	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	440	2.61 (2.58, 2.64)	0.32	1.75, 3.82	2.40	2.62	2.81	32
60 to 69	375	2.47 (2.43, 2.51)	0.34	1.27, 3.88	2.24	2.45	2.71	19
70 to 79	354	2.40 (2.37, 2.44)	0.34	1.29, 3.36	2.16	2.39	2.61	38
80 to 93	79	2.33 (2.26, 2.41)	0.32	1.44, 3.12	2.05	2.39	2.53	21
All	1248	2.49 (2.47, 2.51)	0.34	1.27, 3.88	2.26	2.48	2.72	110

Figures represent distance between anterior lens capsule and corneal endothelium in the pupillary axis.

* Excluding 47 right aphakic or pseudohakic eyes. Reasons for missing data included home visit, not able to undergo testing (Parkinsonism, paralysis) and the first 3 days optical pachymetry was not performed for every subject.

Table 18- Ultrasound lens thickness in phakic subjects (ultrasound biometry - right eyes) *

Men	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	193	4.11 (4.02, 4.20)	0.63	2.61, 5.40	3.61	4.14	4.63	17
60 to 69	164	4.27 (4.16, 4.38)	0.70	2.62, 5.74	3.57	4.39	4.88	6
70 to 79	157	4.27 (4.15, 4.39)	0.74	3.1, 5.56	3.54	4.35	4.91	16
80 to 93	29	4.36 (4.06, 4.67)	0.81	3.13, 5.52	3.72	4.49	5.02	12
All	543	4.22 (4.16, 4.28)	0.70	2.61, 5.74	3.57	4.31	4.81	51
Women								
50 to 59	244	4.15 (4.08, 4.23)	0.59	3.1, 5.65	3.59	4.30	4.62	18
60 to 69	217	4.32 (4.22, 4.41)	0.70	2.95, 5.44	3.26	4.54	4.86	7
70 to 79	203	4.45 (4.35, 4.55)	0.72	3.09, 5.66	3.75	4.70	5.01	16
80 to 93	48	4.51 (4.29, 4.73)	0.76	3.12, 5.70	3.65	4.67	5.13	11
All	712	4.31 (4.26, 4.36)	0.69	2.95, 5.70	3.64	4.50	4.84	52
Men and women								
50 to 59	437	4.13 (4.08, 4.19)	0.61	2.61, 5.65	3.59	4.26	4.62	35
60 to 69	381	4.30 (4.23, 4.37)	0.70	2.95, 5.74	3.56	4.47	4.86	13
70 to 79	360	4.37 (4.29, 4.45)	0.74	3.09, 5.66	3.64	4.56	4.97	32
80 to 93	77	4.46 (4.28, 4.63)	0.77	3.12, 5.70	3.65	4.65	5.09	23
All	1255	4.27 (4.23, 4.31)	0.69	2.61, 5.74	3.59	4.42	4.83	103

* Excluding 47 right aphakic or pseudohakic eyes.

Reasons for missing data included inability to perform measurements during a home visit, or subjects not being able to undergo testing (Parkinsonism, paralysis etc).

Table 19- Ultrasound axial length in phakic subjects (ultrasound biometry - right eyes) *

Men	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	193	23.49 (23.30, 23.70)	1.42	20.18, 31.21	22.72	23.37	23.95	17
60 to 69	164	23.79 (23.55, 24.04)	1.56	21.69, 31.06	22.84	23.41	24.25	6
70 to 79	157	23.44 (23.27, 23.61)	1.05	21.62, 30.97	22.84	23.30	23.88	16
80 to 93	29	23.67 (23.21, 24.21)	1.20	22.14, 27.71	23.11	23.61	24.09	12
All	543	23.58 (23.46, 23.69)	1.36	20.18, 31.21	22.81	23.38	24.01	51
Women								
50 to 59	244	23.08 (22.91, 23.25)	1.33	20.18, 29.93	22.32	22.83	23.42	18
60 to 69	217	23.08 (22.91, 23.25)	1.28	20.8, 30.88	22.31	22.87	23.61	7
70 to 79	203	23.10 (22.90, 23.30)	1.47	20.11, 31.42	22.32	22.80	23.44	16
80 to 93	48	22.94 (22.71, 23.17)	0.80	21.18, 25.24	22.39	22.97	23.39	11
All	712	23.08 (22.98, 23.17)	1.33	20.11, 31.42	22.32	22.84	23.47	52
Men and women								
50 to 59	437	23.26 (23.13, 23.39)	1.38	20.18, 31.21	22.44	23.07	23.74	35
60 to 69	381	23.39 (23.24, 23.53)	1.45	20.8, 31.06	22.52	23.13	23.86	13
70 to 79	360	23.25 (23.11, 23.38)	1.31	20.11, 31.42	22.48	23.09	23.71	32
80 to 93	77	23.22 (22.98, 23.45)	1.03	21.18, 27.71	22.46	23.11	23.65	23
All	1255	23.30 (23.22, 23.37)	1.37	20.11, 31.42	22.48	23.11	23.77	103

* Excluding 47 right aphakic or pseudohakic eyes.

Reasons for missing data included inability to perform measurements during a home visit, or subjects not being able to undergo testing (Parkinsonism, paralysis etc).

Table 20- Mean relative lens position in phakic eyes (Right eyes)

Men	N	Mean (95%CI)	SD	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	193	0.204	0.015	0.194	0.203	0.214	17
60 to 69	164	0.199	0.017	0.189	0.201	0.211	6
70 to 79	157	0.197	0.017	0.186	0.198	0.209	16
80 to 93	29	0.196	0.018	0.186	0.198	0.206	12
All	543	0.200	0.017	0.189	0.201	0.212	51
Women							
50 to 59	244	0.200	0.014	0.190	0.201	0.210	18
60 to 69	217	0.198	0.017	0.188	0.199	0.209	7
70 to 79	203	0.198	0.018	0.186	0.201	0.211	16
80 to 93	48	0.197	0.015	0.187	0.199	0.206	11
All	712						52
Men and women							
50 to 59	437	0.201	0.015	0.191	0.202	0.212	35
60 to 69	381	0.198	0.017	0.188	0.200	0.210	13
70 to 79	360	0.198	0.018	0.186	0.200	0.210	32
80 to 93	77	0.197	0.016	0.186	0.198	0.206	23
All	1255	0.199	0.016	0.189	0.200	0.210	103

* Exclude aphakia and pseudophakic eyes.

Table 21- Ultrasound central corneal thickness in phakic subjects (ultrasound biometry - right eyes) *

Men	N	Mean (95%CI)	SD	Range (Min, Max)	25th Percentile	50th Percentile	75th Percentile	Missing
50 to 59	194	549 (544,553)	34	356, 628	529	551	569	16
60 to 69	163	543 (538, 548)	32	413, 628	523	541	565	7
70 to 79	157	535 (529, 542)	39	461, 758	513	533	553	16
80 to 93	29	533 (521, 544)	31	472, 581	506	527	556	12
All	543	542 (539, 245)	35	356, 758	521	543	564	51
Women								
50 to 59	241	545 (541, 549)	32	395, 655	523	542	567	21
60 to 69	217	541 (537, 545)	31	461, 699	520	540	564	7
70 to 79	203	540 (535, 546)	38	335, 725	515	541	559	16
80 to 93	48	532 (522, 542)	34	468, 636	517	528	557	11
All	709	542 (539, 544)	34	335, 725	519	540	564	55
Men and women								
50 to 59	435	546 (543,549)	33	356, 655	525	547	568	37
60 to 69	380	542 (539, 545)	32	413, 699	521	540	564	14
70 to 79	360	538 (534, 542)	39	335, 758	515	537	556	32
80 to 93	77	532 (525, 540)	33	468, 636	512	528	556	23
All	1252	542 (540,544)	35	335, 758	520	541	564	106

* Excluding 47 right aphakic or pseudohakic eyes, Reasons for missing included inability to measure during home visit, not able to undergo testing (such as Parkinson syndrome, paralysis etc) and not measurable (such as pterygium, corneal diseases). One case after epikeratoplasty was excluded.

Table 22- Gonioscopic angle width (mean and SD of Shaffer grades 0-4) in phakic subjects (static gonioscopy - right eyes) *

Men	N	Superior	Inferior	Average	Missing
50 to 59	205	3.5 (0.8)	3.6 (0.7)	3.6 (0.7)	5
60 to 69	165	2.9 (1.4)	3.1 (1.1)	3.0 (1.2)	5
70 to 79	167	2.5 (1.4)	2.9 (1.1)	2.7 (1.2)	6
80 to 93	34	2.4 (1.4)	2.8 (1.2)	2.6 (1.2)	7
All	571	3.0 (1.3)	3.2 (1.0)	3.1 (1.1)	23
Women					
50 to 59	257	3.0 (1.2)	3.3 (0.9)	3.1 (1.0)	5
60 to 69	222	2.3 (1.4)	2.7 (1.1)	2.5 (1.2)	2
70 to 79	215	1.9 (1.4)	2.3 (1.2)	2.1 (1.3)	4
80 to 93	54	1.9 (1.3)	2.3 (1.3)	2.1 (1.3)	5
All	748	2.4 (1.4)	2.8 (1.2)	2.6 (1.3)	16
Men and women					
50 to 59	462	3.2 (1.0)	3.4 (0.8)	3.3 (0.9)	10
60 to 69	387	2.5 (1.4)	2.9 (1.1)	2.7 (1.2)	7
70 to 79	382	2.2 (1.4)	2.6 (1.2)	2.4 (1.3)	10
80 to 93	88	2.1 (1.4)	2.5 (1.3)	2.3 (1.3)	12
All	1319	2.6 (1.4)	3.0 (1.1)	2.8 (1.2)	39

* Excluding all aphakic and pseudophakic eyes, the angle width was graded using the Shaffer system.

Table 23- Gonioscopic grading of apparent point of first contact between iris and corneoscleral coat (right eyes) *

Men	N	Superior					Inferior					Missi **
Grades†		A	B	C	D	E	A	B	C	D	E	
50 to 59	205	3 (1.5)	8(3.9)	81(39.5)	91(44.2)	22(10.7)	0(0.0)	3(1.5)	59(28.8)	118(57.6)	25(12.2)	5
60 to 69	168	13(7.7)	28(16.7)	56(33.3)	58(34.5)	13(7.7)	2(1.2)	10 (6.0)	63 (37.5)	78(46.4)	15(8.9)	2
70 to 79	168	15(8.9)	35(20.8)	72(42.9)	40(23.8)	6(3.6)	2(1.2)	12(7.1)	92(54.8)	53(31.6)	9(5.4)	5
80 to 93	34	1 (2.9)	9 (26.5)	18 (52.9)	5 (14.7)	1 (2.9)	0(0.0)	3(8.8)	20(58.8)	10(29.4)	1(2.9)	7
All	575	32(5.6)	80(13.9)	227(39.5)	194(33.7)	42(7.3)	4(0.7)	28(4.9)	234(40.7	259 (45.0)	50(8.7)	19
Women												
50 to 59	258	12(4.7)	37(14.3)	115(44.6)	84(32.6)	10(3.9)	2(0.8)	4(1.6)	106(41.1)	135(52.3)	11(4.3)	4
60 to 69	223	17(7.6)	60(26.9)	89(39.9)	48(21.5)	9(4.0)	3(1.4)	18(8.1)	112(50.2)	82(36.8)	8(3.6)	1
70 to 79	217	41(18.9)	54(24.9)	81(37.3)	38(17.5)	3(1.4)	6(2.8)	26(12.0)	118(54.4)	59(27.2)	8(3.7)	2
80 to 93	57	11(19.3)	18(31.6)	20(35.1)	8(14.0)	0(0.0)	4(7.0)	8(14.0)	33(57.9)	11(19.3)	1(1.8)	2
All	755	81(10.7)	169(21.4)	305(40.4)	178(23.6)	22(2.9)	15(2.0)	56(7.4)	369(48.9)	287(38.0)	28(3.7)	9
Men and women												
50 to 59	463	15(3.2)	45(9.7)	196(42.3)	175(37.8)	32(6.9)	2(0.4)	7(1.5)	165(35.6)	253(54.6)	36(7.8)	9
60 to 69	391	30(7.7)	88(22.5)	145(37.1)	106(27.1)	22(5.6)	5(1.3)	28(7.2)	175(44.8)	160(40.9)	23(5.9)	3
70 to 79	385	56(14.6)	89(23.1)	153(39.7)	78(20.2)	9(2.3)	8(2.1)	38(9.9)	210(54.6)	112(29.1)	17(4.4)	7
80 to 93	91	12(13.2)	27(29.7)	38(41.8)	13(14.3)	1(1.0)	4(4.4)	11(12.1)	53(58.2)	21(23.1)	2(2.2)	9
All	1330	113(8.5)	249(18.7)	532(40.0)	372(28.0)	64(4.8)	19(1.4)	84(6.3)	603(45.3)	546(41.1)	78(5.9)	28

* Excluding all 47 aphakic and pseudophakic eyes.

** Reasons for missing data included: home visit (16), refusal(2), not suitable for measurement (4), corneal opacity (4), unknown/missing (2).

† Grade based on iris insertion on Spaeth grading system: A-anterior to Schwalbe's line, B-behind the Schwalbe's line; C-scleral spur; D-Deep: into the ciliary body; E-extremely deep: in ciliary body.

Table 24- Gonioscopic iris insertion grade by proportion of Grade A and B (Apparent iris insertion on static, right eyes) *

Men	N	Superior	Nasal	Inferior	Temporal
50 to 59	205	5.4	1.0	1.5	1.5
60 to 69	168	24.4	12.5	7.1	11.3
70 to 79	168	29.8	11.9	8.3	16.7
80 to 93	34	29.4	14.7	8.8	20.6
All	575	19.5	8.4	5.6	9.9
Women					
50 to 59	258	19.0	7.4	2.3	7.4
60 to 69	223	34.5	14.8	9.4	18.8
70 to 79	217	43.8	21.2	14.8	24.9
80 to 93	57	50.9	24.6	21.1	29.8
All	755	33.1	14.8	9.4	17.5
Men and women					
50 to 59	463	12.96	4.5	1.9	4.8
60 to 69	391	30.18	13.8	8.4	15.6
70 to 79	385	37.66	17.1	11.9	21.3
80 to 93	91	42.86	20.9	16.5	26.4
All	1330	27.22	12.0	7.7	14.2

* Excluding 47 aphakic and pseudohakic eyes

Table 25- Gonioscopic grading of "True" point of first contact between iris and corneoscleral coat (right eyes) *

Men	N	Superior N(%)					Inferior N(%)					Missi **
Grades		A	B	C	D	E	A	B	C	D	E	
50 to 59	205	0(0.0)	0(0.0)	43(21.0)	134(65.4)	28(13.7)	0(0.0)	0(0.0)	20(9.8)	151(73.7)	34(46.6)	5
60 to 69	168	2(1.2)	1(0.6)	53(31.6)	94(55.9)	18(10.7)	1(0.6)	0(0.0)	29(17.3)	120(71.4)	18(10.7)	2
70 to 79	168	4(2.4)	0(0.0)	64(38.1)	89(53.0)	11(6.6)	1(0.6)	0(0.0)	35(20.8)	114(67.9)	18(10.7)	5
80 to 93	34	0(0.0)	0(0.0)	19(55.9)	13(38.2)	2(5.9)	0(0.0)	0(0.0)	11(32.4)	21(61.8)	2(5.9)	7
All	575	6(1.0)	1(0.2)	179(31.1)	330(57.4)	59(10.3)	2(0.35)	0(0.0)	95(16.52)	406(70.61)	72(12.5)	19
Women												
50 to 59	258	0(0.0)	2(0.8)	76(29.5)	164(63.6)	16(6.2)	0(0.0)	0(0.0)	36(13.9)	206(79.8)	16(6.2)	4
60 to 69	223	2(0.9)	1(0.5)	97(43.5)	114(51.1)	9(4.0)	1(0.5)	0(0.0)	50(22.4)	161(72.2)	11(4.9)	1
70 to 79	217	5(2.3)	0(0.0)	102(47.0)	105(48.4)	5(2.3)	1(0.5)	1(0.5)	66(30.4)	136(62.7)	13(6.0)	2
80 to 93	57	0(0.0)	1(1.8)	31(54.4)	24(42.1)	1(1.8)	1(1.8)	0(0.0)	20(35.1)	33(57.9)	3(5.3)	2
All	755	7(0.93)	4(0.53)	306(40.5)	407(53.9)	31(4.1)	3(0.4)	1(0.1)	172(22.8)	536(80.0)	43(5.7)	9
Men and women												
50 to 59	463	0(0.0)	2(0.4)	119(25.7)	298(64.4)	44(9.5)	0(0.0)	0(0.0)	56(12.1)	357(77.1)	50(10.8)	9
60 to 69	391	4(1.0)	2(0.5)	150(38.4)	208(53.2)	27(6.9)	2(0.5)	0(0.0)	79(20.2)	281(71.9)	29(7.4)	3
70 to 79	385	9(2.3)	0(0.0)	166(43.1)	194(50.4)	16(4.2)	2(0.5)	1(0.3)	101(26.2)	250(64.9)	31(8.1)	7
80 to 93	91	0(0.0)	1(1.1)	50(54.9)	37(40.7)	3(3.3)	1(1.1)	0(0.0)	31(34.1)	54(59.3)	5(5.5)	9
All	1339	13(1.0)	5(0.4)	485(36.5)	737(55.4)	90(6.8)	5(0.4)	1(0.1)	267(20.1)	942(70.8)	115(8.7)	28

* Excluding all 47 aphakic and pseudophakic eyes

** Reasons for missing data include: home visit preventing full examination (16), refusal (2), not suitable for measurement (4), corneal opacity (4), unknown/missing (4). † Grade based on iris insertion on Spaeth grading system: A-anterior to Schwalbe's line, B-behind the Schwalbe's line; C-scleral spur; D-Deep: into the ciliary body; E-extremely deep: in ciliary body.

Table 26- Gonioscopic iris profile in phakic subjects (static gonioscopy, right eyes) *

Men	N	Steep	Regular	Queer	Plateau	Missing
50 to 59	205	22 (10.8)	160 (78.8)	15 (7.4)	6 (3.0)	7
60 to 69	168	40 (23.9)	102 (61.1)	8 (4.8)	17 (10.2)	3
70 to 79	168	61 (36.5)	87 (52.1)	0 (0.0)	19 (11.4)	6
80 to 93	34	16 (47.1)	14 (41.2)	0 (0.0)	4 (11.8)	7
All	575	139 (24.3)	363 (63.6)	23 (4.0)	46 (8.1)	23
Women						
50 to 59	258	66 (26.0)	166 (65.4)	8 (3.2)	14 (5.5)	8
60 to 69	223	93 (41.7)	97 (43.5)	2 (0.9)	31 (13.9)	1
70 to 79	217	112 (51.9)	70 (32.4)	2 (0.9)	32 (14.8)	3
80 to 93	57	27 (48.2)	19 (33.9)	0 (0.0)	10 (17.9)	3
All	755	298 (39.8)	352 (47.0)	12 (1.6)	87 (11.6)	15
Men and women						
50 to 59	463	88 (19.3)	326 (71.3)	23 (5.0)	20 (4.4)	15
60 to 69	391	133 (34.1)	199 (51.0)	10 (2.6)	48 (12.3)	4
70 to 79	385	173 (45.2)	157 (41.0)	2 (0.5)	51 (13.3)	9
80 to 93	91	43 (47.8)	33 (36.7)	0 (0.0)	14 (15.6)	10
All	1330	437 (33.1)	715 (54.2)	35 (2.7)	133 (10.1)	38

* Excluding 47 aphakic and pseudohakic eyes
Figures are N (%)

Table 27- Proportion (%) of iris profile by mean Shaffer angle width in phakic right eyes

Mean Shaffer Grades **	N	Steep‡	Regular‡	Concave‡	Plateau‡
0	51	70.6	1.9	0	27.5
1	142	68.3	0.7	0	31.0
2	209	69.9	12.0	0	18.1
3	379	35.4	58.3	0.3	6.1
4	529	3.2	88.3	6.4	2.1
Total	1310	32.8	54.6	2.67	9.9

* Excluding 47 aphakic and pseudohakic eyes

** The average of Shaffer grades in superior and inferior quadrants were taken, and re-classified this into Grade 0=0; Grade 1=0.5~1; Grade 2=1.5~2; Grade 3=2.5~3, Grade 4=3.5~4.

‡ Data is presented as proportion by row.

Table 28 – Gonioscopic characteristics of phakic right eyes with PAS

	N	n (Cases with PAS)	Percent of PAS * (95%CI)	Odds ratio (95%CI) **
Shaffer angle width†				
4	534	0	0.0 (0, 0.7)	---
3	381	1	0.3 (0, 1.5)	1.0
2	211	4	1.9 (0.7, 4.8)	13.2 (1.36, 127.4)
1	143	18	12.6 (8.1, 19.0)	123.3 (16.3, 934.6)
0	51	14	27.5 (17.1, 40.9)	345.8 (44.29, 2700.4)
Number of quadrants with pigmented TM not visible				
0	948	1	0.1 (0, 0.6)	1.0
1	149	2	1.3 (0.4, 4.8)	6.4 (0.4, 102.9)
2	87	4	4.6 (1.8, 11.2)	45.6 (5.0, 413.0)
3	92	14	15.2 (9.3, 23.9)	155.8 (20.1, 1206.7)
4	54	16	29.6 (19.1, 42.8)	398.7 (51.5, 3085.4)

* PAS – peripheral anterior synechiae, TM-trabecular meshwork.

** Odds ratios are calculated referring the Shaffer grade 3 and zero quadrants with pigmented TM not visible as baseline.

† Mean of angle width in superior and inferior quadrants: Mean gonioscopic angle width was calculated by adding Shaffer grades in superior and inferior quadrants divided by 2, recoded as 0=0 1 = 0.25 to 1.25, 2= 1.5 to 2.25, 3= 2.5 to 3.25, 4= 3.5 to 4

Table 29- Association of gonioscopic angle width / iris insertion with biometry, age, sex and BMI. (Right eyes) mean (SD)

Mean Shaffer grades	Anterior Chamber Depth (mm) By optical pachymetry	Lens thickness (mm, Ultrasound)	Axial length (mm, ultrasound)	Relative lens position	Corneal power in diopters	Refractive Spherical equivalent (D)	Body Mass Index (Kg / m^2)	Height (m)	Age in years	Sex ratio (Male: Female)
4	2.73 (0.26)	4.05 (0.59)	23.79 (1.52)	0.200 (0.017)	43.79 (1.40)	-0.98 (2.92)	23.71 (3.03)	1.58(0.08)	61.6	293:241
3	2.49 (0.23)	4.20 (0.70)	23.18 (1.10)	0.198 (0.016)	43.79 (1.41)	-0.41(2.57)	23.85 (3.32)	1.56(0.08)	64.8	158:223
2	2.31 (0.24)	4.44 (0.74)	22.89 (1.31)	0.199 (0.017)	44.31 (1.52)	-0.02 (2.92)	23.28 (3.50)	1.52(0.07)	68.6	63:147
1	2.10 (0.19)	4.80 (0.54)	22.58 (0.73)	0.200 (0.012)	44.04 (1.50)	0.69 (8.03)	23.19 (3.60)	1.53(0.07)	69.5	44:100
0	1.94 (0.28)	4.79 (0.55)	22.69 (1.15)	0.192 (0.021)	43.85 (1.67)	0.10 (2.15)	22.11 (3.55)	1.49 (0.07)	72.3	13:37
All	2.49 (0.34)	4.27 (0.69)	23.29 (1.37)	0.199 (0.017)	43.90 (1.49)	-0.46 (2.76)	23.56 (3.31)	1.56(0.08)	65.1	571:748
Linear coefficient (P value, Model 1) ‡	2.39 (P<0.001)	-0.64 (P<0.001)	0.27 (P<0.001)	4.562 (P=0.026)	-0.06 (P=0.009)	-0.08 (P<0.001)	0.04 (P=0.003)	3.94 (P<0.001)	-0.04 (P<0.001)	
Linear coefficient (P value, Model 2) ‡	2.21 (P<0.001)	-0.550 (P<0.001)	0.25 (P<0.001)	1.23 (P=0.516)	-0.03 (P=0.320)	-0.08 (P<0.001)	0.03 (P=0.003)	1.37 (P=0.030)	---	----
Mean iris insertion										
E	2.85 (0.28)	4.10 (0.59)	24.36 (1.98)	0.202 (0.017)	43.48 (1.48)	-1.62 (3.63)	23.39 (3.26)	1.61(0.07)	61.5	44:22
D	2.69 (0.26)	4.03 (0.60)	23.70 (1.46)	0.198 (0.017)	43.80 (1.41)	-0.89 (2.82)	23.93 (3.12)	1.58(0.08)	62.3	246:245
C	2.42 (0.26)	4.34 (0.71)	23.04 (1.11)	0.200 (0.017)	43.99 (1.43)	-0.15 (2.59)	23.56 (3.33)	1.55(0.08)	65.9	236:369
B	2.04 (0.21)	4.78 (0.59)	22.56 (0.82)	0.197 (0.014)	43.94 (1.59)	0.52 (1.81)	22.67 (3.59)	1.52(0.08)	70.5	46:110
A	1.88 (0.39)	4.53 (0.99)	22.57 (1.75)	0.186 (0.027)	44.42 (1.88)	-1.48 (1.87)	22.63 (3.22)	1.49(0.08)	71.5	3:9
All	2.49 (0.34)	4.27 (0.69)	23.29 (1.37)	0.199 (0.017)	43.90 (1.49)	-0.46 (2.76)	23.56 (3.31)	1.56(0.08)	65.1	571:748

* Excluding all 47 aphakic and pseudophakic eyes, Mean gonioscopic angle width was calculated by adding Shaffer grades in superior and inferior quadrants divided by 2, recoded as 0=0, 1 = 0.25 to 1.25, 2= 1.5 to 2.25, 3= 2.5 to 3.25, 4= 3.5 to 4. Mean iris insertion was calculated by adding the numeric iris insertion values on static status and divided by 4, recoded as A=1 B = 1.25 to 2.25, C= 2.5 to 3.25, D= 3.5 to 4.25, E= 4.5 to 5.

‡ Model 1: age and gender were not included as dependent variables; Model 2: age and gender were included in the linear regression model.

Table 30 – Demographic and refraction characteristics of Cases and Controls*

	Cases § (N=194)	Controls § (N=122)	P*
Age (%) *			
50-59	10.5	40.2	<0.001
60-69	36.7	23.8	
70-79	40.8	31.9	
80+	12.1	4.1	
Mean(SD)	70.0 (8.6)	63.9 (9.6)	<0.001
Sex (%)			
M	33.0	42.6	
F	67.0	57.4	0.084
Refraction (%)			
< -0.5 D	22.9	32.1	0.006
-0.5 ~+2D	62.4	64.3	
> +2D	14.7	3.6	
Mean (SD)	0.5 (1.8)	-0.5 (2.6)	0.002
IOP (mmHg)			
Mean(SD)	15.1 (2.9)	15.1 (2.7)	0.9318
Weight (kg) mean (SD)	53.3 (10.5)	57.5 (10.7)	0.0075
Height (M) mean (SD)	1.53 (0.08)	1.56 (0.09)	0.011
Body Mass Index mean (SD)	22.7 (3.4)	23.5 (3.3)	0.095

* The data are presented as a proportion over the total (by column).

§ Cases: subjects had occludable angle (posterior, usually pigmented, trabecular meshwork being not visible in at least 2 quadrants) in right eyes; Controls: a systematic sample (1 in 10 consecutive) of subjects who didn't meet the criteria to be considered a "case" in the right eye.

Table 31 – Biometric characteristics of Cases and Controls*

	Cases § (N=194)	Controls § (N=122)	P‡
ACD (mm)			
Mean (SD)	2.09 (0.21)	2.57 (0.33)	<0.0001
Median (range)	2.11 (1.44, 2.65)	2.59 (1.85, 3.88)	
Axial length (mm)			
Mean (SD)	22.52 (0.76)	23.46 (1.45)	<0.0001
Median (range)	22.45 (20.18, 25.09)	23.30 (20.18, 31.42)	
Lens thickness (mm)			
Mean (SD)	4.78 (0.55)	4.27 (0.67)	<0.0001
Median (range)	4.88 (3.09, 5.74)	4.39 (2.95, 5.7)	
Relative lens position (units)			
Mean (SD)	0.199 (0.014)	0.201 (0.017)	0.3631
Median (range)	0.200 (0.152, 0.230)	0.202 (0.146, 0.244)	
Corneal refractive power (D)			
Mean (SD)	44.09 (1.60)	44.07 (1.54)	0.9256
Median (range)	43.97 (40.25, 48.31)	43.87 (40.69, 49.06)	

* The available number of cases: ACD 310, axial length 307, lens thickness 306, corneal curvature 355; relative lens position 306 in the whole subjects (316 subjects).
‡ Unpaired Student's t test

Table 32 – Gonioscopic characteristics of Cases and Controls*

	Cases (N=194)	Controls (N=118)	P ‖
Shaffer grade angle width [Mean (SD)]			
Superior quadrant	0.5 (0.7)	2.9 (1.2)	<0.0001
Inferior quadrant	1.2 (0.9)	3.2 (0.8)	<0.0001
True iris insertion [%] §			
Superior quadrants			
C	87.6	34.8	<0.0001
D	12.4	57.6	
E	0	7.6	
Inferior quadrant			
C	55.7	11.9	<0.0001
D	44.3	77.1	
E	0	11.0	
Iris Profile [%] §			
Steep	67.0	34.8	<0.0001
Plateau	33.0	5.9	
Regular	0.0	55.9	
Concave	0.0	3.4	

* Six aphakic and pseudophakic eyes were excluded. Apparent iris insertion was not analyzed because it was used as the criterion for assignment to the case/control groups.

‡ Student's t test was used for angle width comparison; Chi-square test was used in true iris insertion and profile. .

§Data presented as proportions.

‖ Chi square test for iris insertion and profile, Wilcoxon rank test for Shaffer angle width.

Table 33 – Conventional penlight oblique test in right eyes of Cases and Controls*

	Cases	Controls	P‡
N §	179	101	
Deep (%)	0.6	31.7	<0.0001
Medium (%)	20.7	48.5	
Shallow (%)	78.8	19.8	

* Oblique penlight test: Deep: the whole nasal iris is illuminated, Medium: anywhere between pupil margin and mid peripheral iris is illuminated; Shallow: only pupil margin is illuminated. Data is presented as proportion by column.
§ Fifteen cases and 17 controls were missing data. Six aphakic and pseudophakic eyes were excluded.
‡ Chi square test

Table 34 –Slit lamp oblique test in right eyes of Cases and Controls*

	Cases	Controls	P‡
N	189	105	
Band length (graticule units)			
Mean(SD)	81.4 (2.5)	82.0 (2.2)	0.05
Median (range)	81 (70, 90)	82 (75, 90)	
Shadow length (graticule units)			
Mean(SD)	16.7 (3.6)	10.8 (3.5)	<0.001
Median(range)	17 (1, 25)	10 (2, 19)	
Ratio (Shadow / band length)			
Mean (SD)	0.21 (0.04)	0.13 (0.05)	<0.001
Median (range)	0.20 (0.01, 0.30)	0.13 (0.02, 0.22)	

* Slit lamp oblique test used to measure, 1) Band length: from the nasal limbus to temporal limbus; 2) shadow length: distance of margin of shadow to nasal limbus. The ratio was calculated as the shadow length divided by the band length.
‡ Unpaired student test.

Table 35 – van-Herick limbal chamber depth grade estimated with reference to standard photos in right eyes of Cases and Controls*

Grades	Cases (N=188)	Controls (N=104)	P‡
0%	2.1	0	<0.0001
5%	44.2	3.8	
15%	35.6	9.6	
25%	14.4	17.3	
40%	2.1	26.9	
75%	1.1	24.0	
100%	0.5	18.3	

* van-Herick test was evaluated by using standard photos. Data is presented as proportion (%) by column.
‡ Wilcoxon rank sum test.

Table 36 – Limbal chamber depth measurement using eyepiece measuring graticule and the van Herick technique in cases and controls*

	Cases	Controls	P‡
N	189	105	
Peripheral corneal thickness (graticule units)			
Mean(SD)	11.7 (1.1)	12.1 (1.2)	0.009
Median (range)	12 (9, 15)	12 (9, 15)	
Peripheral anterior chamber depth (graticule units)			
Mean(SD)	2.6 (1.3)	6.6 (3.6)	<0.0001
Median(range)	2 (0, 11)	5 (1, 18)	
Ratio			
Mean (SD)	0.22 (0.11)	0.54 (0.3)	<0.0001
Median (range)	0.18 (0.0, 1.0)	0.45 (0.08, 1.38)	

* Examination method was similar to traditional van-Herick test, but slit lamp reticule eyepiece was used to measure the corneal thickness and peripheral anterior chamber depth.
‡ Unpaired student test.

Table 37 – Characteristics of subjects who did and did not attend for UBM examination*

	Narrow angle **			Normal controls			All		
	Examined	Unexamined	P*	Examined	Unexamined	P	Examined	Unexamined	P
Age									
50-59	15 (12.6)	5 (6.9)		29 (42.7)	20 (37.0)		44 (23.5)	25 (19.8)	
60-69	47 (39.5)	23 (31.9)		17 (25.0)	12 (22.2)		64 (34.2)	35 (27.8)	
70-79	51 (42.9)	27 (37.5)		20 (29.4)	19 (35.2)		71 (38.0)	46 (36.5)	
80+	6 (5.0)	17 (23.6)		2 (2.9)	3 (5.6)		8 (4.3)	20 (15.9)	
Subtotal	119 (100)	72 (100)	0.002	68 (100)	54 (100)	0.765	187 (100)		0.005
Sex									
M	79 (66.4)	48 (66.7)		39 (57.4)	31 (57.4)		118 (63.1)	79 (62.7)	
F	40 (33.6)	24 (33.3)	0.968	29 (42.7)	23 (42.6)	0.995	69 (36.9)	47 (37.3)	0.942
ACD									
Mean	2.11	2.05		2.59	2.59		2.28	2.28	
SD	0.20	0.20	0.08	0.36	0.36	0.970	0.36	0.39	0.934
Shaffer									
Mean‡	1.1	1.1		3.1	3.1		2.0	1.8	
SD	0.8	0.8	0.765	0.9	0.8	0.823	1.3	1.3	0.244

* Enrollment based on static gonioscopy: narrow angles were defined as those with at least 2 quadrants where the posterior, pigmented trabecular meshwork was not visible. Normal controls were selected systematically from those classified as not having narrow angles.
**Unpaired Student's test for comparison of age, ACD and Shaffer grades, Chi square test for the comparison of sex variable.
‡ Mean of Shaffer grades of superior and inferior quadrants

Table 38 Reproducibility of UBM image acquisition and analysis

	Image Analysis				Image acquisition			
	1st	2nd	Diff	95% LOA	1st	2nd	Diff	95% LOA *
AOD250 §								
Superior	0.033(0.013)	0.038(0.013)	-0.006	(-0.041, 0.040)	0.033(0.014)	0.054(0.020)	-0.022	(-0.173, 0.129)
Nasal	0.111(0.025)	0.111(0.026)	0.001	(-0.033, 0.053)	0.111*(0.025)	0.071*(0.024)	0.041	(-0.080, 0.162)
Inferior	0.058(0.017)	0.059(0.015)	-0.001	(-0.039, 0.024)	0.058(0.017)	0.048(0.012)	0.010	(-0.104, 0.124)
Temporal	0.099(0.020)	0.089(0.018)	0.010	(-0.069, 0.070)	0.099(0.020)	0.099(0.021)	0.000	(-0.089, 0.090)
AOD500								
Superior	0.052(0.017)	0.051(0.016)	0.008	(-0.032, 0.034)	0.052(0.017)	0.072(0.018)	-0.019	(-0.101, 0.062)
Nasal	0.133(0.028)	0.129(0.029)	0.004	(-0.072, 0.080)	0.133(0.028)	0.109(0.028)	0.024	(-0.073, 0.121)
Inferior	0.079(0.020)	0.087(0.020)	-0.008	(-0.058, 0.042)	0.079(0.020)	0.066(0.016)	0.013	(-0.059, 0.085)
Temporal	0.120*(0.024)	0.105*(0.023)	0.014	(-0.026, 0.054)	0.120(0.024)	0.118(0.022)	0.001	(-0.088, 0.090)
TCPD								
Superior	0.528(0.038)	0.518(0.038)	0.010	(-0.071, 0.090)	0.528(0.038)	0.547(0.037)	-0.019	(-0.200, 0.162)
Nasal	0.581(0.023)	0.593(0.021)	-0.013	(-0.120, 0.095)	0.581(0.023)	0.599(0.029)	-0.018	(-0.146, 0.109)
Inferior	0.563(0.024)	0.561(0.023)	0.002	(-0.094, 0.098)	0.563(0.024)	0.539(0.030)	0.023	(-0.073, 0.119)
Temporal	0.547(0.021)	0.583(0.028)	-0.036	(-0.316, 0.245)	0.547(0.021)	0.546(0.015)	0.001	(-0.159, 0.161)
IT750								
Superior	0.421(0.013)	0.422(0.013)	-0.001	(-0.087, 0.085)	0.421(0.013)	0.428(0.016)	-0.007	(-0.091, 0.076)
Nasal	0.450(0.019)	0465(0.019)	-0.015	(-0.102, 0.072)	0.450(0.019)	0.449(0.020)	0.001	(-0.060, 0.062)
Inferior	0.426*(0.021)	0.461*(0.018)	-0.036	(-0.146, 0.075)	0.426(0.021)	0.429(0.028)	0.004	(-0.139, 0.131)
Temporal	0.428(0.016)	0.450(0.020)	-0.021	(-0.100, 0.058)	0.428(0.016)	0.442(0.020)	-0.014	(-0.070, 0.043)
ARA								
Superior	0.724(0.032)	0.693(0.031)	0.032	(-0.131, 0.194)	0.725(0.032)	0.708(0.035)	0.017	(-0.215, 0.249)
Nasal	0.658(0.033)	0.668(0.040)	-0.011	(-0.143, 0.121)	0.658(0.033)	0.675(0.037)	-0.017	(-0.186, 0.152)
Inferior	0.668(0.027)	0.703(0.026)	-0.035	(-0.260, 0.191)	0.668(0.0.027)	0.687(0.040)	-0.018	(-0.334, 0.297)
Temporal	0.678(0.033)	0.685(0.033)	-0.007	(-0.149, 0.135)	0.678(0.033)	0.695(0.028)	-0.017	(-0.155, 0.121)
Curvature								
Superior	15.902*(2.608)	10.52*(1.432)	5.382	(-7.975, 18.739)	15.902(2.608)	15.323(3.742)	0.580	(-28.323, 29.481)
Nasal	9.374(1.345)	9.060(1.475)	0.314	(-7.686, 8.314)	9.374(1.345)	10.901(2.081)	-1.528	(-12.003, 8.948)
Inferior	10.370(1.994)	9.472(1.160)	0.898	(-9.292, 11.088)	10.370(1.994)	10.840(1.238)	-0.469	(-10.945, 10.007)
Temporal	13.208(2.382)	16.154(3.956)	-2.945	(-30.549, 24.659)	13.208(2.382)	12.001(1.723)	1.208	(-17.925, 20.341)

* LOA: Limit of agreement was calculated as per Bland, JM. Measurement error. Br Med J 1996;312:p1654 § AOD250; AOD500=anterior opening distance at 250 or 500 microns to scleral spur, TCPD= trabecular ciliary process distance; IT750=iris thickness at 750 microns to scleral spur; ARA=anterior recess area; curvature=curvature of posterior surface of the iris

Table 39- Major UBM variables in eyes with occludable angles ("cases") and normal controls (UBM Pro 2000 software, mean of 4 quadrants, right eyes) *

	Cases § (N=119)	Controls § (N= 68)	P‡
AOD 250 (mm) §			
Mean (SD)	0.047 (0.038)	0.090 (0.053)	<0.0001
Median (range)	0.039 (0.000, 0.200)	0.080 (0.000, 0.190)	
AOD500 (mm)			
Mean (SD)	0.054 (0.042)	0.152 (0.087)	<0.0001
Median (range)	0.044 (0.000, 0.191)	0.137 (0.000, 0.327)	
Anterior recess area (ARA)			
Mean (SD)	0.044 (0.028)	0.105 (0.105)	<0.0001
Median (range)	0.036 (0.001, 0.138)	0.094 (0.009, 0.213)	
Iris insertion to scleral spur			
Mean (SD)	0.101 (0.064)	0.120 (0.059)	0.059
Median (range)	0.091 (0.006, 0.266)	0.116 (0.000, 0.235)	

* All variables are based on the mean of the specific parameters on 4 quadrants.
§ AOD: angle opening distance; AOD250: angle opening distance at the location with 250 microns distance to scleral spur. Iris insertion to scleral spur: measured by the linear distance from iris insertion to the scleral spur.
‡ Unpaired student t test

Table 40- Major UBM parameters in eyes with narrow angles and control eyes (self-developed software, mean of 4 quadrants, right eyes) *

	Cases § (N=119)	Controls § (N= 68)	P‡
AOD 250 (mm)			
Mean (SD)	0.089 (0.0503)	0.130 (0.064)	<0.0001
Median (range)	0.085 (0.000, 0.228)	0.131 (0.000, 0.303)	
AOD500 (mm)			
Mean (SD)	0.106 (0.054)	0.183 (0.079)	<0.0001
Median (range)	0.096 (0.000, 0.256)	0.185 (0.000, 0.374)	
Area ratio of iris and angle			
Mean (SD)	0.62 (--)	0.53 (--)	<0.0001
Median (range)	0.54 (0.39, 0.83)	0.54 (0.37, 0.75)	
Iris thickness at 500 (mm)			
Mean (SD)	0.371 (0.051)	0.378 (0.055)	0.397
Median (range)	0.375 (0.258, 0.521)	0.378 (0.277, 0.516)	
Iris thickness at 1000 (mm)			
Mean (SD)	0.405 (0.050)	0.415 (0.058)	0.247
Median (range)	0.410 (0.283, 0.549)	0.416 (0.291, 0.536)	
Iris curvature radius (mm)			
Mean (SD)	5.47 (1.47)	8.42 (6.02)	<0.0001
Median (range)	5.3 (2.98, 11.53)	6.88 (2.25, 14.96)	

* All variables are based on the mean of the specific parameters on 4 quadrants.
§ AOD: anterior opening distance; AOD250: anterior opening distance at the location with 250 microns distance to scleral spur;
‡ Unpaired Student's t test

Table 41- Range of UBM major parameters in "normal" right eyes *

	Superior	Nasal	Inferior	Temporal	P
N	61	61	61	61	
AOD 250 (mm)					
Mean (SD)	0.072(0.056)	0.125(0.075)	0.099(0.078)	0.130(0.084)	
Median	0.061	0.131	0.080	0.118	
AOD500 (mm)					
Mean (SD)	0.115(0.072)	0.175(0.091)	0.144(0.102)	0.178(0.102)	
Median	0.113	0.174	0.125	0.174	
ARA750 (mm)					
Mean (SD)	0.078(0.051)	0.114(0.065)	0.108(0.068)	0.129(0.067)	
Median	0.066	0.123	0.095	0.123	
SS-IR (mm)					
Mean (SD)	0.089(0.083)	0.133(0.078)	0.113(0.091)	0.156(0.081)	
Median	0.083	0.078	0.091	0.081	
TCPD (mm)					
Mean (SD)	0.615(0.094)	0.658(0.092)	0.659(0.105)	0.650(0.099)	
Median	0.612	0.644	0.664	0.645	
Area ratio of iris and angle					
Mean (SD)	0.67 (0.11)	0.60(0.12)	0.61(0.12)	0.62(0.13)	
Median	0.68	0.61	0.63	0.61	
Iris thickness at 750 (mm)					
Mean (SD)	0.445(0.089)	0.445(0.093)	0.446(0.081)	0.451(0.079)	
Median	0.450	0.449	0.451	0.446	
Iris thickness at 1000 (mm)					
Mean (SD)	0.474(0.084)	0.495(0.071)	0.493(0.083)	0.476(0.074)	
Median	0.472	0.507	0.504	0.488	
Iris curvature radius (mm)					
Mean (SD)	6.37(4.31)	6.42(3.29)	6.25(6.75)	6.78(6.16)	
Median	5.33	5.70	6.05	6.06	

* Eyes that do not meet the criteria of narrow angle defined as pigmented TM not visible in 2 or more quadrants.

Table 42- Association of gonioscopic angle width with major parameters in UBM measurements in all cases and controls cases

Mean Shaffer grades	N	AOD250*	AOD500*	ARA750*	Iris insertion*	Area ratio*	Iris thickness 500*	Iris thickness 1000*	Iris convexity
4	26	0.114 (0.051)	0.202 (0.088)	0.135 (0.051)	0.141 (0.056)	0.51	0.387 (0.054)	0.421 (0.055)	11.48 (7.71)
3	20	0.071 (0.056)	0.107 (0.080)	0.080 (0.050)	0.105 (0.067)	0.55	0.367 (0.066)	0.397 (0.065)	6.26 (1.90)
2	39	0.052 (0.042)	0.074 (0.047)	0.055 (0.032)	0.103 (0.048)	0.59	0.379 (0.048)	0.416 (0.044)	5.72 (1.85)
1	67	0.049 (0.036)	0.059 (0.041)	0.047 (0.029)	0.101 (0.063)	0.63	0.365 (0.047)	0.405 (0.049)	5.35 (1.19)
0	22	0.043 (0.036)	0.035 (0.041)	0.035 (0.026)	0.102 (0.055)	0.62	0.376 (0.058)	0.398 (0.061)	5.21 (4.51)
All	174	0.061 (0.048)	0.086 (0.077)	0.064 (0.048)	0.108 (0.062)	0.59	0.373 (0.052)	0.408 (0.052)	6.46 (3.93)
Regression coefficientp §		0.017 (P<0.001)	0.039 (P<0.001)	0.024 (P<0.001)	0.009 (P=0.023)	-0.03 (P<0.001)	0.004 (P=0.234)	0.004 (P=0.178)	1.44 (P<0.001)

* AOD: anterior opening distance; ARA:anterior recess area; Iris insertion: distance between iris insertion to scleral spur; Area ratio: cumulative area of iris versus area with boundary of posterior surface of cornea and anterior surface of ciliary process; Iris thickness: iris thickness at given distance to scleral spur.

§ Linear regression model

Table 43. Qualitative grading of UBM images in case and controls (superior quadrant, right eyes)

Proportion (%)	Cases (N=118)	Controls (N=58) §	P‡
Ciliary body size			
Small	26.5	30.5	0.749
Medium	44.4	42.4	
Large	29.1	27.1	
Ciliary body rotation			
Neutral	40.1	36.2	
Anterior	59.9.	63.8	0.721
Iris position			
Basal	64.4	65.5	
Middle	33.1	32.8	
Apical	2.5	1.7	0.940
Iris angulation			
None	72.0	67.2	
Mild	20.4	22.4	
Pronounced	7.6	10.4	0.762
Iris thickness, basal			
Thin	24.6	36.2	
Medium	58.5	34.5	
Thick	16.9	29.3	0.011
Iris thickness, overall			
Thin	4.2	5.2	
Medium	64.4	58.6	
Thick	31.4	36.2	0.755
Iris convexity			
Absent	2.5	8.6	
Mild	82.2	74.1	
Moderate	15.3	17.3	
Extreme			0.167

*Data are presented as proportions by column. The grading is based on standard photos (Method section).
‡ Chi Square test for the difference of frequency trend

Table 44. Proportion of eyes with irido-trabecular contact in "case"and "control" groups identified by ultrasound biomicroscopy (right eyes)

	Cases (%) (N=117)	Controls (%) (N=57) §	P‡
Quadrant (%)*			
Superior	78.6 (92/117)	43.9 (16/57)	<0.0001
Nasal	40.2 (47/117)	15.8 (9/57)	0.001
Inferior	59.5 (70/117)	29.3 (17/57)	<0.0001
Temporal	25.6 (30/117)	13.8 (8/57)	0.074
B-type closure (%)**			
Superior	40.2 (37/92)	36.0 (9/16)	0.702
Nasal	38.3 (18/47)	33.3 (3/9)	0.778
Inferior	40.5 (28/70)	5.9(1/17)	0.007
Temporal	26.7 (8/30)	37.5 (3/8)	0.548

*Data are presented as proportions. The grading is based on standard photos (Method section). This figure represents the proportion of appositional closure in the eyes with 3 or more quadrants where it was notpossible to see the posterior (usually pigmented) TM (identified as "cases") and the subjects not meeting this criterion (normal).

§ Appositional closure in less than 2 quadrants can exist in normal control eyes.

** These figures represent the proportion of B-type (denoting basal contact), characterized as an area continuous irido-trabecular contact extending from iris root anteriorly in eyes with appositional closure. This is differentiated from S-type closure where there is an area of contact between iris and corneo-scleral coat, anterior to an aqueous-filled space separating peripheral iris and trabecular meshwork (denoting contact at the level of Schwalbe's line).

Table 45 – Characteristics of those who did and did not undergo laser PI among those with occludable angles *

	Received	Eligible	Participation (%)	P§	Subjects with UBM data‡
Age					
50-59	13 (17.6)	17 (12.1)	76.5	0.055	13
60-69	27 (36.5)	46 (32.9)	58.7		31
70-79	32 (43.2)	57 (40.7)	56.1		37
80+	2 (2.7)	20 (14.3)	10.0		4
Sex					
M	20 (27.0)	32 (26.0)	62.5	0.876	23
F	54 (72.9)	91 (74.0)	59.3		62
Sub-total	74 (100)	140 (100)	53%		85

* The cases have an occludable angle in either eye after excluding those with diagnosis of PAC or PACG in either eye.
** Data in brackets are proportions by column.
§ P value is given by Chi2 test.
‡ All subjects received LPI had UBM data available, because this was the criterion for enrolling subjects.

Table 46– Intraocular pressure and biometric variables before and after laser iridotomy (All eyes) *

	N‡	Mean before LPI (95%CI)	Mean after LPI (95% CI)	Paired difference of Mean	P
IOP (mmHg) §	74	14.3 (13.6, 15.0)	11.3 (10.6, 11.9)	3.1	<0.0001
ACD (mm) **	73	2.04 (2.00, 2.08)	2.04 (1.96, 2.11)	-0.007	0.8061
Lens thickness (mm)	74	4.70 (4.51, 4.89)	4.80 (4.70, 4.90)	0.10	0.2547
Axial length (mm)	74	22.50 (22.28, 22.71)	22.47 (22.27, 22.67)	-0.03	0.4029
Shaffer angle width (Units)					
Superior	71	0.4 (0.2, 0.5)	1.9 (1.6, 2.3)	1.5	<0.0001
Inferior	71	0.9 (0.7, 1.1)	2.8 (2.6, 3.1)	1.9	<0.0001
Overall	71	0.6 (0.5, 0.8)	2.4 (2.1, 2.6)	1.7	<0.0001

* In total, 38 right eyes and 36 left eyes.
** ACD was measured by optical pachymetry, lens thickness and axial length by ultrasound biometry.
‡ N: Number of available records
§ Without using medication influencing IOP for 2 weeks.

Table 47 –Apparent iris insertion (Spaeth Grade) before and after laser peripheral iridotomy

Superior quadrant	After iridotomy (%)				
Before PI	A	B	C	D	Total
A	2 (7.4)	14 (51.9)	8 (29.6)	3 (11.1)	27 (100)
B	3 (7.0)	25 (58.1)	14 (32.6)	1 (2.3)	43 (100)
C	0 (0.0)	0 (0.0)	2 (100)	0 (0.0)	2 (100)
Total	5	39	24	4	72
Nasal quadrant	After iridotomy (%)				
Before PI	A	B	C	D	Total
A	0 (0.0)	2 (28.6)	5 (71.4)	0 (0.0)	7 (100)
B	0 (0.0)	15 (32.6)	27 (58.7)	4 (8.7)	46 (100)
C	0 (0.0)	3 (15.8)	10 (52.6)	6 (31.6)	19 (100)
Total	0	20	42	10	72
Inferior quadrant	After iridotomy (%)				
Before PI	A	B	C	D	Total
A	0 (0.0)	3 (42.9)	2 (28.6)	2 (28.6)	7 (100)
B	1 (3.0)	3 (9.1)	23 (69.7)	6 (18.2)	33 (100)
C	0 (0.0)	5 (15.6)	22 (68.8)	5 (15.6)	32 (100)
Total	1	11	47	13	72
Temporal quadrant	After iridotomy (%)				
Before PI	A	B	C	D	Total
A	0 (0.0)	2 (25.0)	4 (50.0)	2 (25.0)	8 (100)
B	0 (0.0)	12 (22.6)	32 (60.4)	9 (16.8)	53 (100)
C	0 (0.0)	2 (18.2)	9 (81.8)	0 (0.0)	11 (100)
Total	0	16	45	11	72

Table 48 –Number of quadrants with UBM appositional closure before and after laser peripheral iridotomy N(%)

Before laser PI	After laser iridotomy					
	0	**1**	**2**	**3**	**4**	**Total**
0	2 (50.0)	1 (25.0)	1 (25.0)	0	0	4 (5.5)
1	9 (69.2)	4 (30.8)	0	0	0	13 (17.8)
2	11 (55.0)	2 (10.0)	5 (25.0)	2 (10.0)	0	20 (27.4)
3	6 (27.3)	5 (22.7)	6 (27.3)	3 (13.6)	1 (4.6)	22 (30.1)
4	2 (15.4)	2 (15.4)	2 (15.4)	5 (38.5)	2 (15.4)	13 (17.8)
Total	30 (41.1)	14 (19.2)	15 (20.6)	10 (13.7)	3 (4.1)	72 (100)

UBM qualitative data was available for 72 eyes after laser PI.

Table 49 – UBM anterior opening distances before and after laser peripheral iridotomy* [Mean(SD)]

	Before	After	Paired difference	% of changes‡	P value
N	72	72			
AOD 250 (mm)					
Superior	0.037 (0.045)	0.058 (0.059)	0.021 (0.007)	+57%	0.003
Nasal	0.081 (0.071)	0.106 (0.075)	0.025 (0.068)	+31%	0.002
Inferior	0.040 (0.041)	0.057 (0.058)	0.017 (0.062)	+43%	0.021
Temporal	0.096 (0.078)	0.122 (0.072)	0.025 (0.075)	+27%	0.005
Mean	0.064 (0.052)	0.085 (0.052)	0.021 (0.037)	+33%	<0.001
AOD500 (mm)					
Superior	0.032 (0.040)	0.082 (0.068)	0.050 (0.066)	+156%	<0.0001
Nasal	0.086 (0.076)	0.129 (0.079)	0.044 (0.065)	+50%	<0.0001
Inferior	0.051 (0.059)	0.086 (0.066)	0.034 (0.067)	+69%	<0.0001
Temporal	0.096 (0.062)	0.147 (0.071)	0.051 (0.066)	+53%	<0.0001
Mean	0.067 (0.046)	0.111 (0.059)	0.044 (0.042)	+66%	<0.0001
Angle recess area(mean)	0.040 (0.030)	0.070 (0.036)	0.029 (0.025)	+75%	<0.0001
Area ratio (iris/angle)	0.71 (0.07)	0.69 (0.07)	0.014	-3%	0.076

* UBM data was available for 72 eyes before and after laser iridotomy, after excluding the PAC/PACG cases. ‡ Percentage of changing after laser PI, "+" stands for increase and "-"stands for a decrease after iridotomy.

Table 50. UBM measurements of ciliary body and iris before and after laser iridotomy* [Mean(SD)]

	Before	After	Paired difference	P value (Paired t test)
N	72	72		
TCPD (mm)	0.537 (0.060)	0.561 (0.060)	0.024 (0.046)	0.0001
ICPD (mm)	0.120 (0.063)	0.081 (0.034)	-0.039 (0.054)	<0.0001
SS-IR (mm)	0.105 (0.074)	0.118 (0.070)	0.013 (0.046)	0.017
IT 750 (mm)	0.440 (0.047)	0.459 (0.102)	0.020 (0.012)	0.094
IT 1000 (mm)	0.471 (0.054)	0.488 (0.006)	0.017 (0.034)	0.0001
Radius of iris curvature (mm)				
Superior	4.80 (1.62)	13.72 (18.68)	8.92	0.0001
Nasal	4.79 (1.66)	12.54 (9.63)	7.75	<0.0001
Inferior	5.40 (2.10)	16.08 (11.80)	10.67 (11.96)	<0.0001
Temporal	5.02 (1.58)	10.87 (14.84)	5.84 (14.85)	0.0014
Mean	5.02 (1.26)	13.31 (7.71)	8.29 (7.59)	<0.0001

* UBM data is available in 72 laser PI postoperative eyes after excluding the PAC/PACG cases.
TCPD: Trabecular-ciliary process distance; ICPD: Iris ciliary process distance; SS-IR: Scleral spur and iris insertion distance; IT: iris thickness

Table 51. Qualitative grades of iridociliary anatomy from UBM images before and after peripheral iridotomy [Presented as proportions].

	Before	After	P value‡
N	72	72	
Ciliary rotation			
Neutral	27.8	13.9	
Anterior	72.2	86.1	0.091
Iris insertion			
Basal	61.1	51.4	
Middle	38.9	48.6	0.002
Apex	0	0	
Iris angulation			
None	68.1	83.3	
Mild	20.8	15.3	
Pronounced	11.1	1.4	0.078
Iris convexity			
Absent	2.8	73.6	
Mild	77.8	26.4	
Moderate	18.1	0	
Extreme	1.4	0	0.005

‡ Chi square test for the difference of frequency trend

Table 52. UBM characteristics in eyes with angles remaining closed after laser iridotomy*

	Open after PI	Closed after PI	P‡
N	58	14	
AOD250 (mm)	0.071 (0.042)	0.049 (0.052)	0.099
AOD500 (mm)	0.108 (0.057)	0.052 (0.038)	0.001
Iris insertion to SS (mm)	0.125 (0.069)	0.085 (0.069)	0.061
Area recess area (mm)	0.076 (0.035)	0.042 (0.029)	0.002
Iris thickness at 500	0.376 (0.045)	0.399 (0.043)	0.095
Iris thickness at 1000	0.415 (0.052)	0.447 (0.035)	0.041
TCPD at 500 um (mm)	0.562 (0.068)	0.514 (0.046)	0.033
ICPD at 500 um (mm)	0.078 (0.032)	0.075 (0.035)	0.781

* Number of total eyes received laser PI with occludable angle: 74, excluding the PAC and PACG cases. Gonioscopy and UBM data are missing in 2 cases.

‡ Unpaired t test

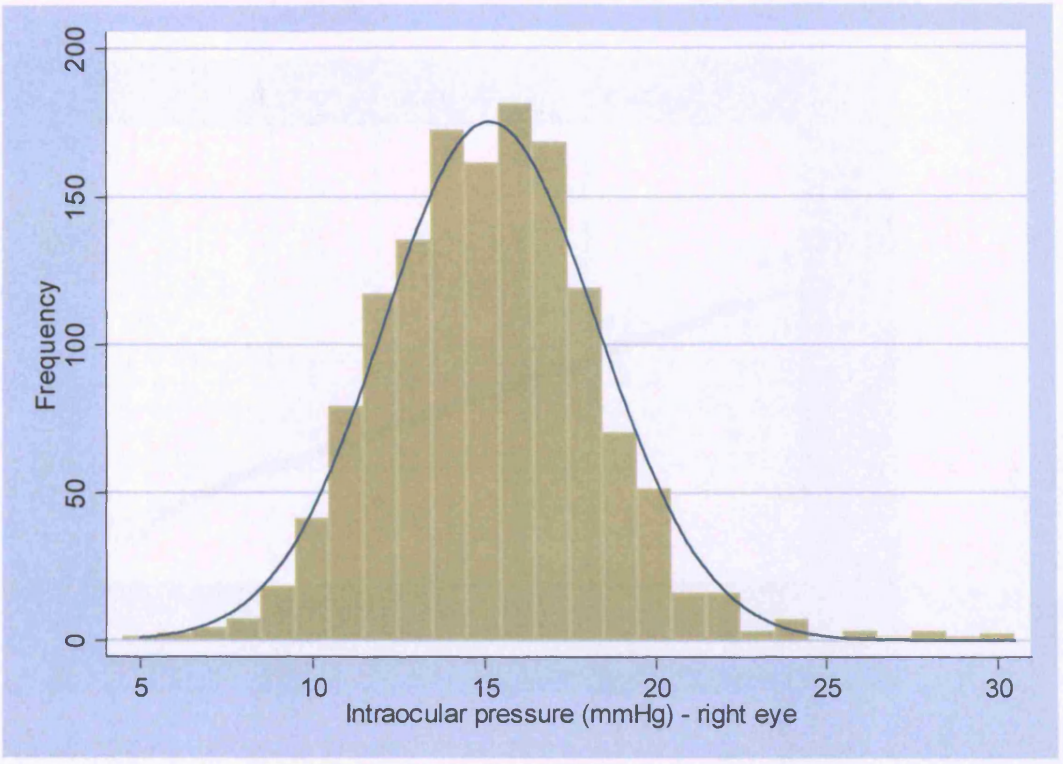


Figure 21 Distribution of IOP (mmHg) on the right eyes for all subjects.

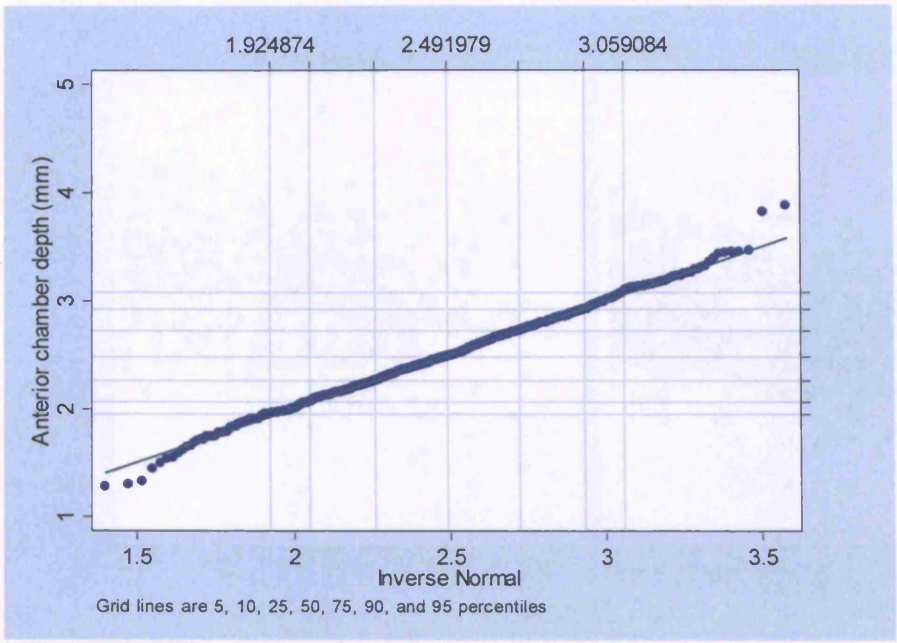


Figure 22 Q-Q plot of quantiles of ACD against the quantiles of normal distribution.

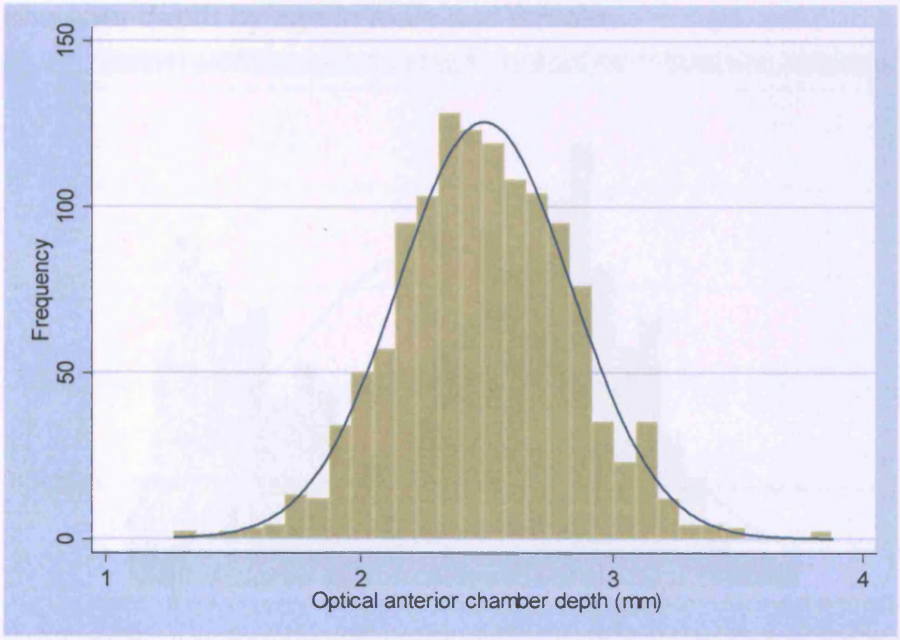


Figure 23. Distribution of optical anterior chamber depth (mm) on the phakic right eyes.

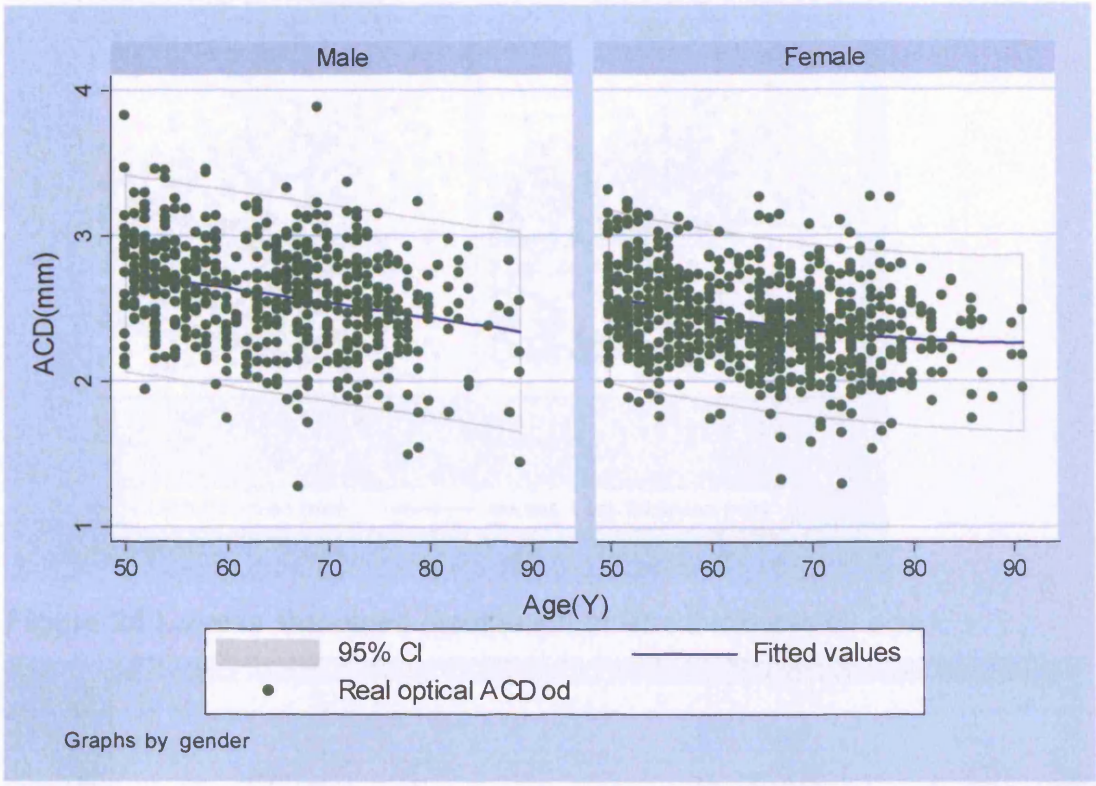


Figure 24 Quadratic regression curve (with 95% interval) for axial anterior chamber depth by age in male and female.

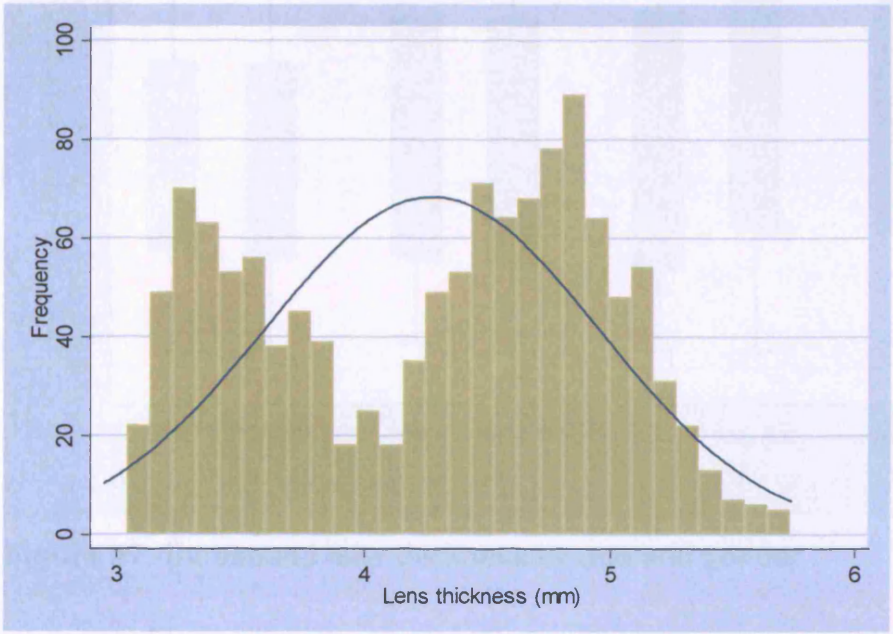


Figure 25 Distribution of lens thickness on phakic eyes.

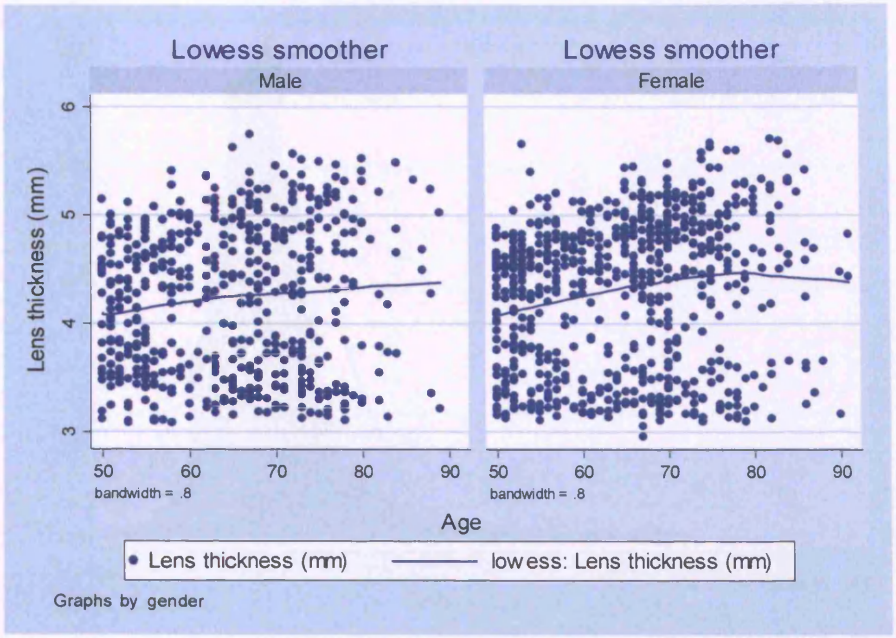


Figure 26 Lowess smoothed distribution of lens thickness by age.

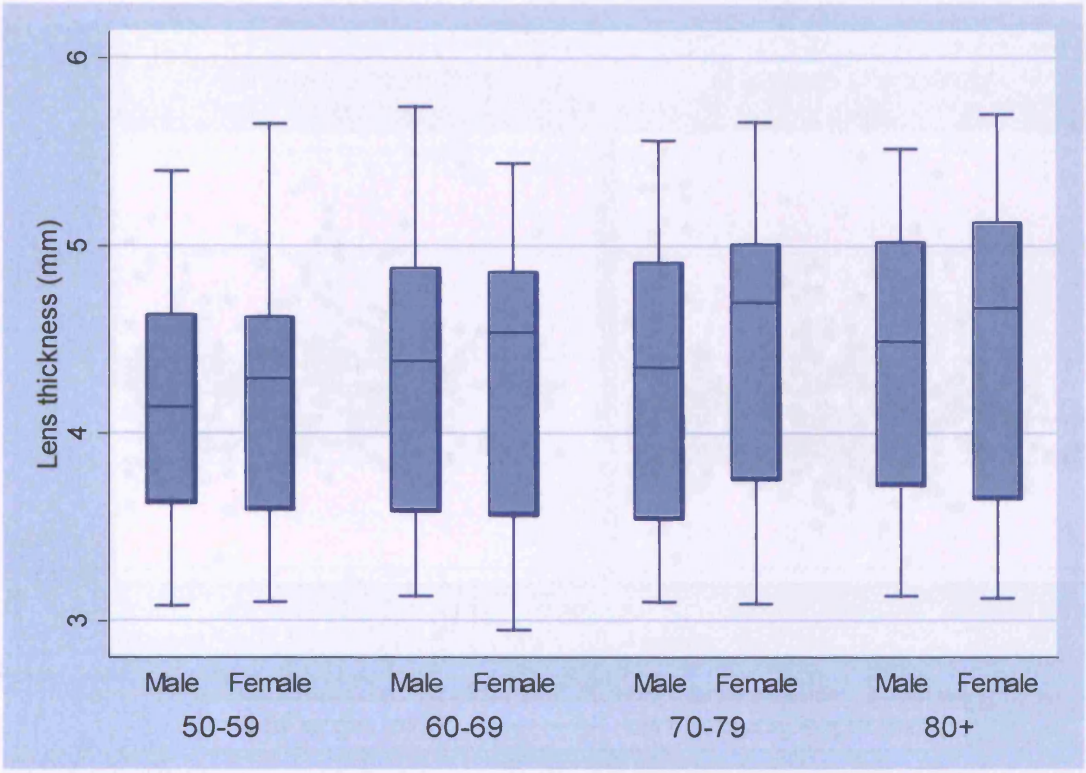


Figure 27. Ultrasound lens thickness by age and gender.

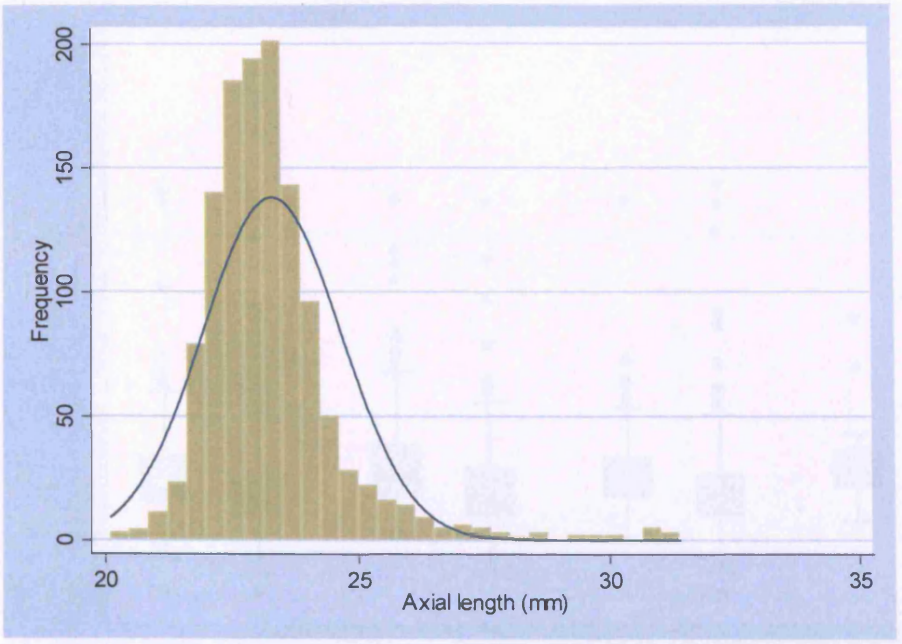


Figure 28 Distribution of axial length on the phakic eyes (Right eyes)

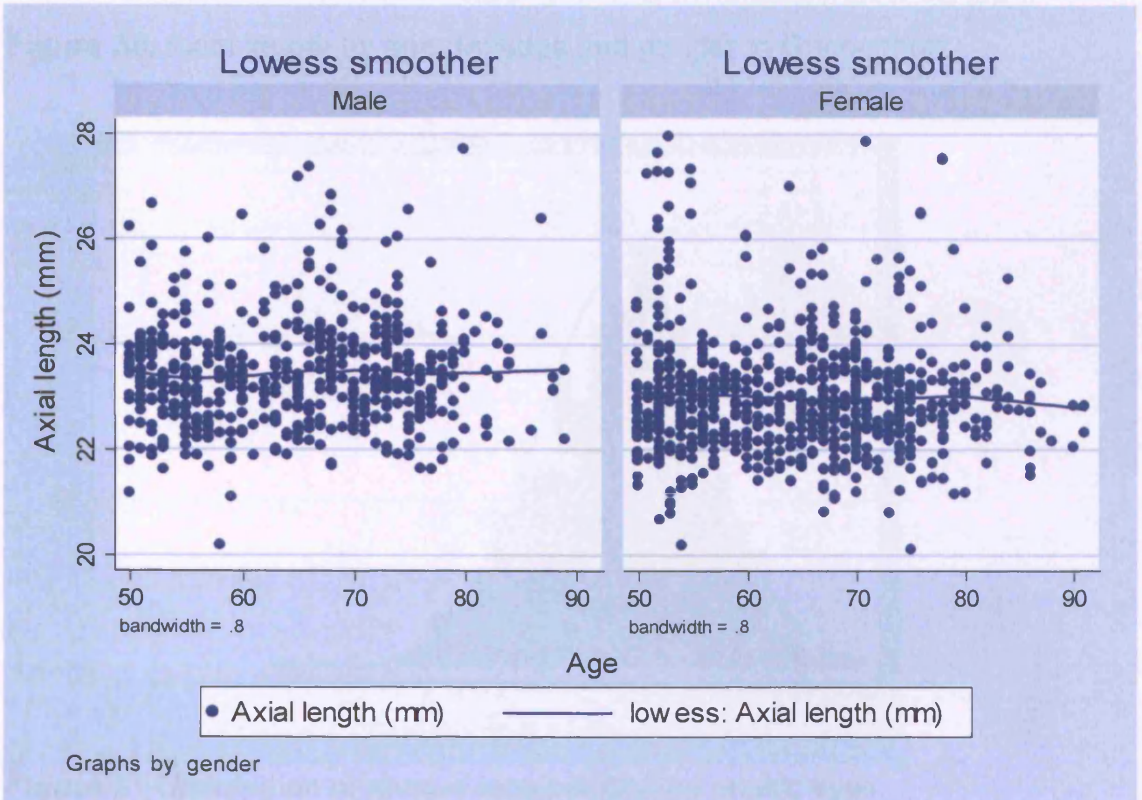


Figure 29 Lowess smoothed distribution of axial length by age in men and women after excluding aphakia and those with greater than 28mm (extreme outliers).

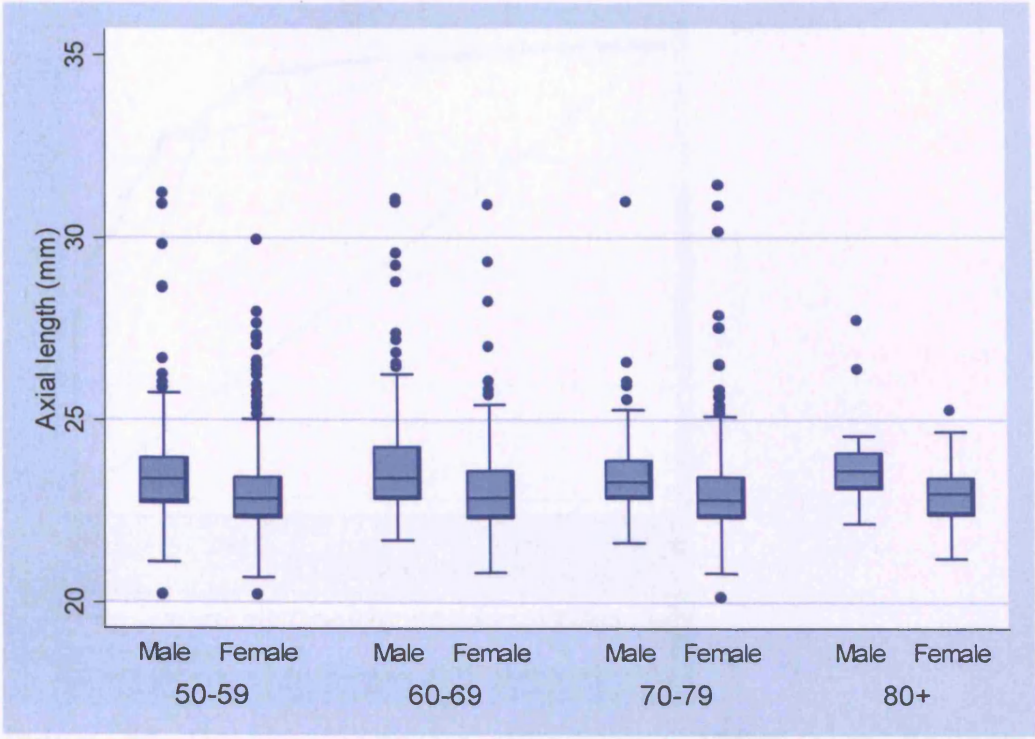


Figure 30. Axial length by age decades and gender in Guangzhou.

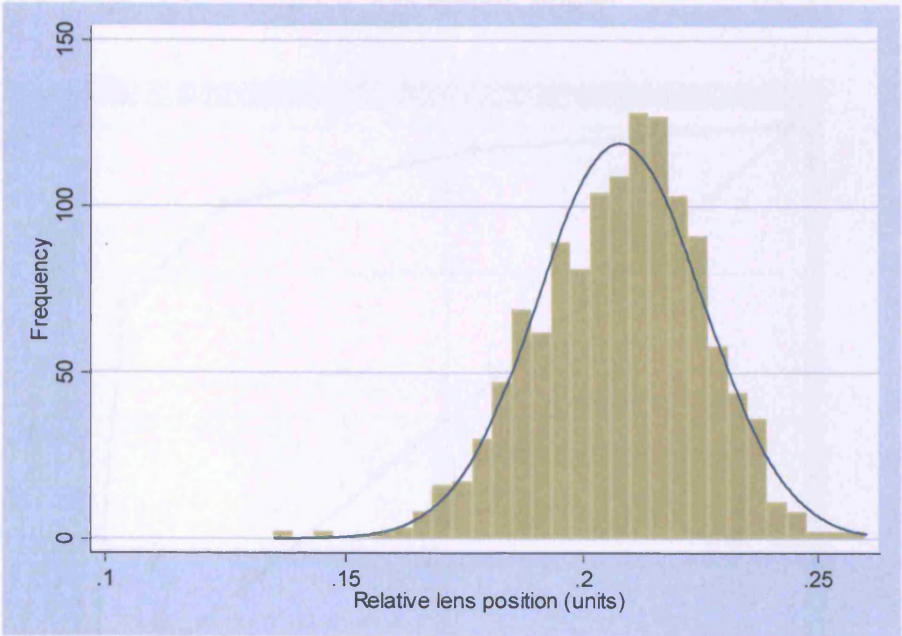


Figure 31 Distribution of relative lens position on phakic eyes.

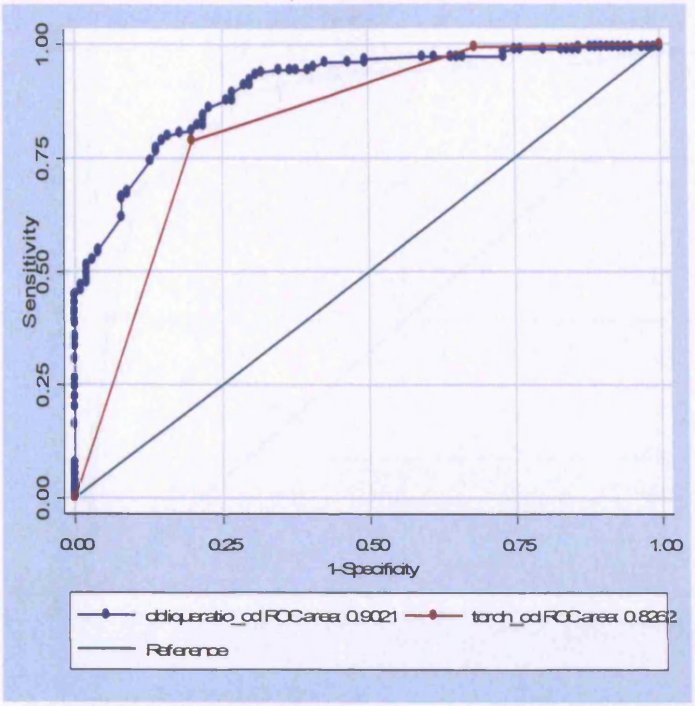


Figure 32. Receiver operating characteristic (ROC) curve for detection of occludable angles by conventional penlight oblique test and slit lamp sidelight test on differentiating the occludable angle.

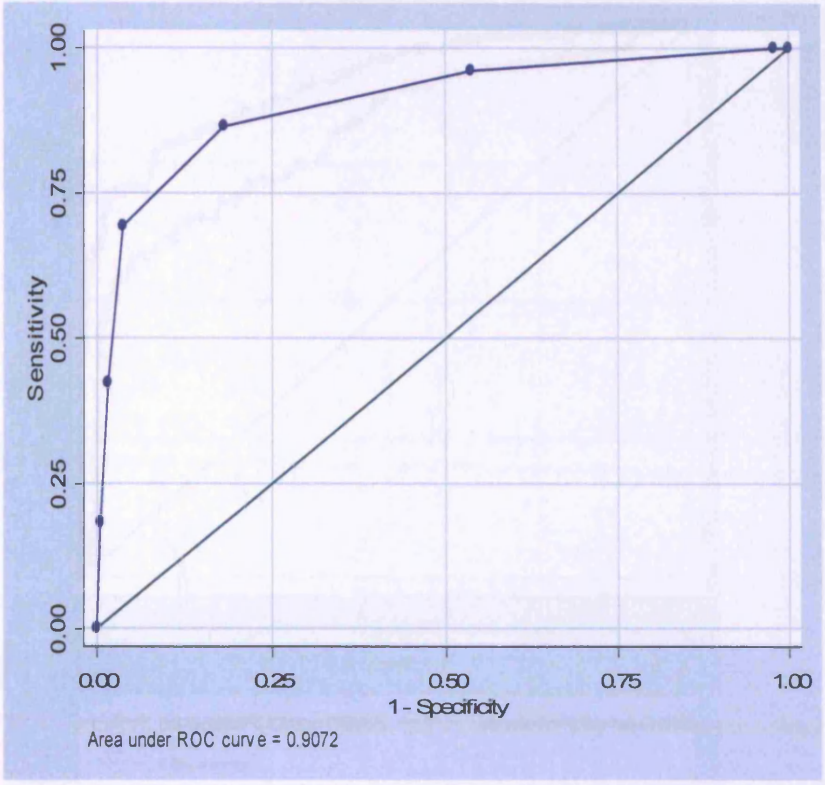


Figure 33 Receiver operating characteristic (ROC) curve for detection of occludable angles by for van-Herick with standard photos method.

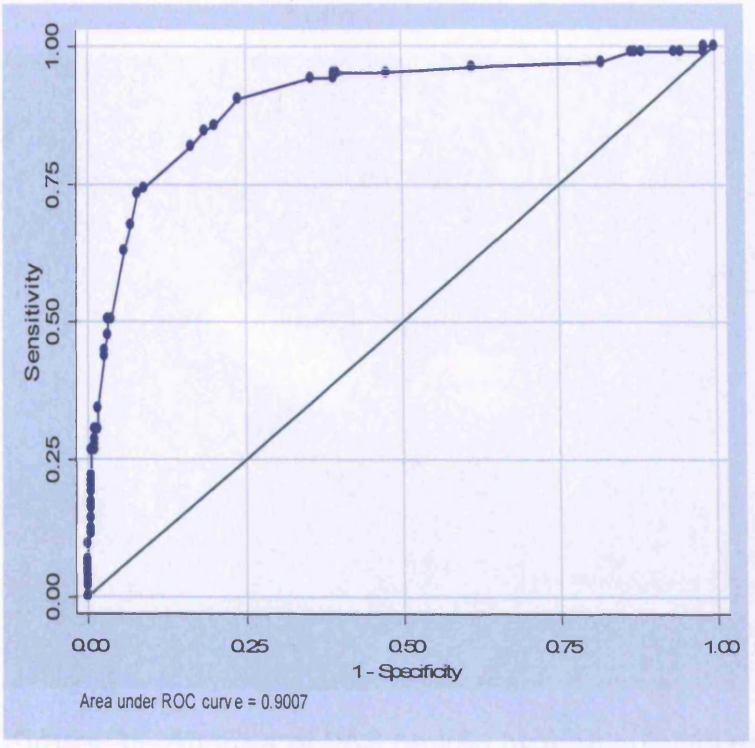


Figure 34 Receiver operating characteristic (ROC) curve for detection of occludable angles by measurement of limbal chamber depth (van Herick technique) using an eyepiece measuring graticule

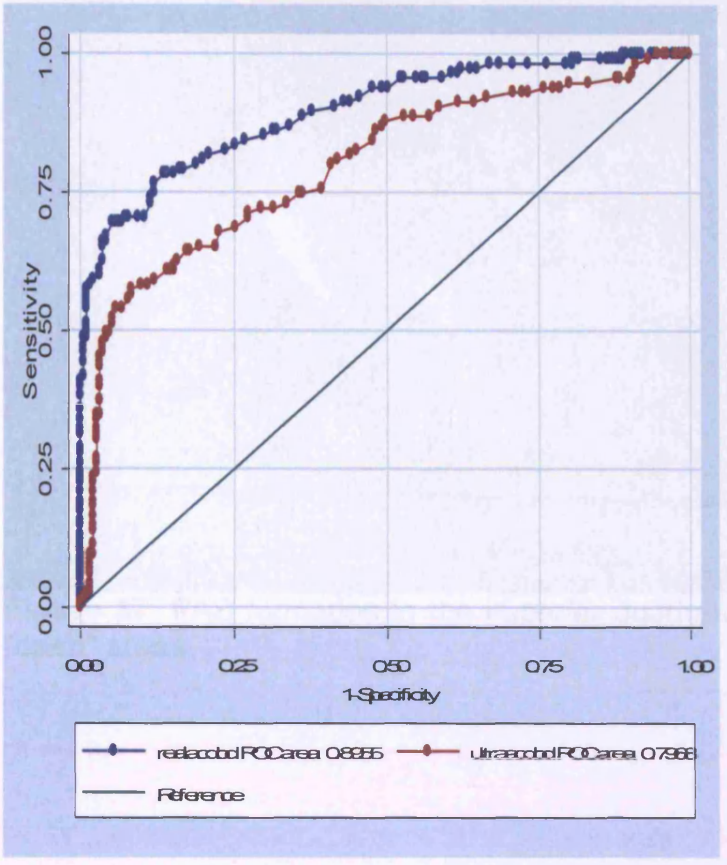


Figure 35 Receiver operating characteristic (ROC) curve for detection of occludable angles by optical and ultrasonic pachymetry ACD.

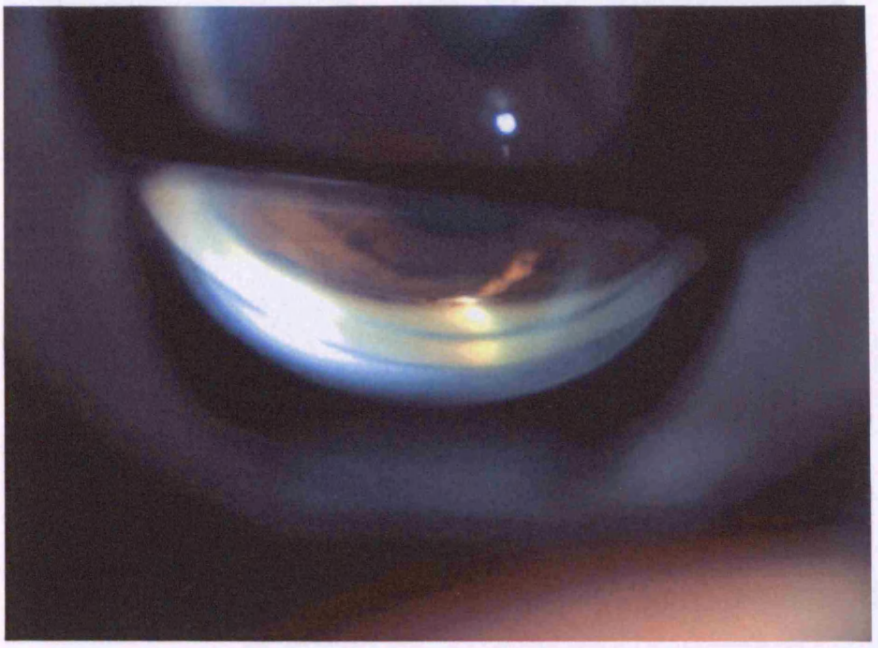


Figure 36. An area of PAS broken by manipulative gonioscopy. The appositional closure and early PAS formation is evident from the blotchy pigmentation on the TM in the superior quadrant.

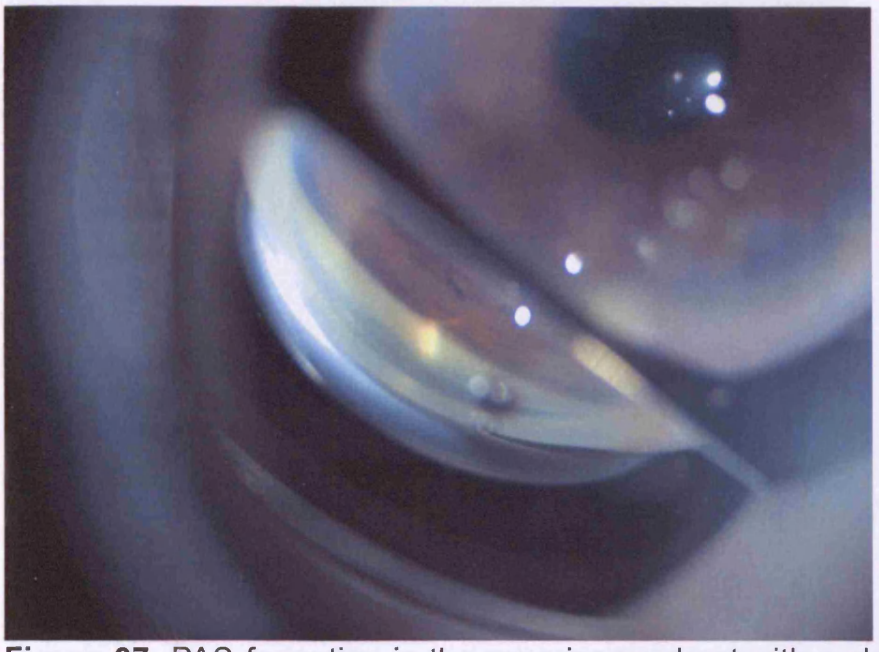


Figure 37. PAS formation in the superior quadrant with a clear border with the "open" areas.

Figure 38. This photograph illustrates transition between different degrees of PAS.

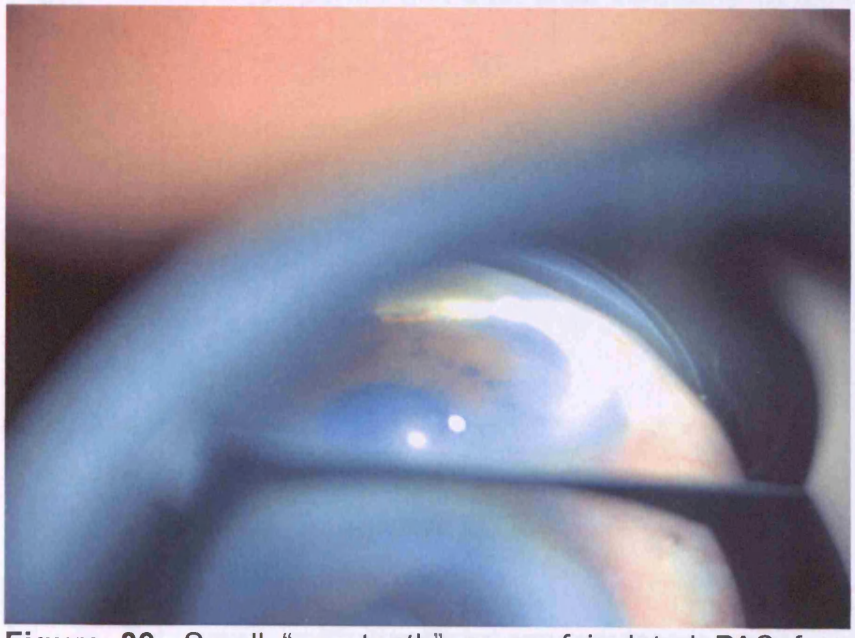


Figure 39. Small "saw-tooth" area of isolated PAS formation in the inferior quadrant.

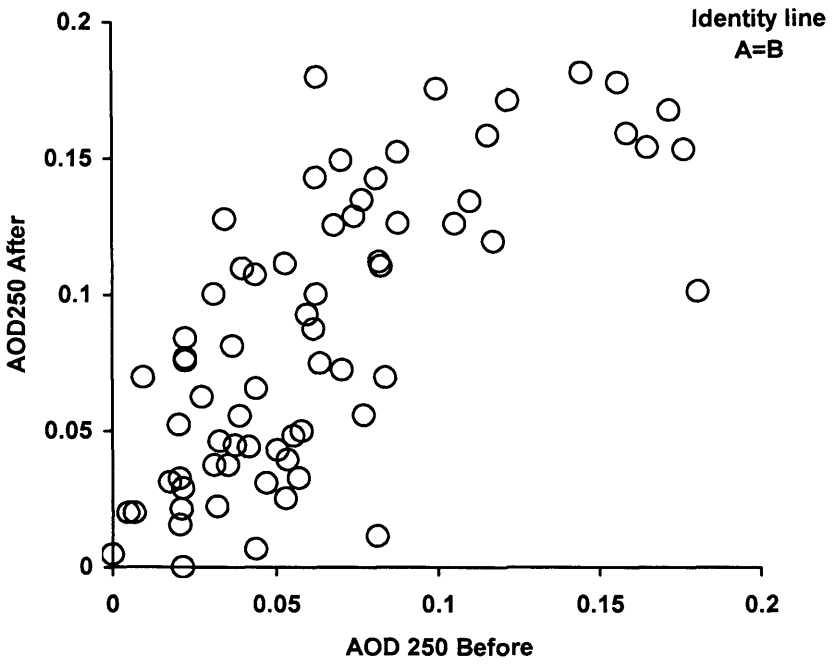


Figure 40. AOD250 before and after laser iridotomy. (X axis: before; Y axis: after laser PI)

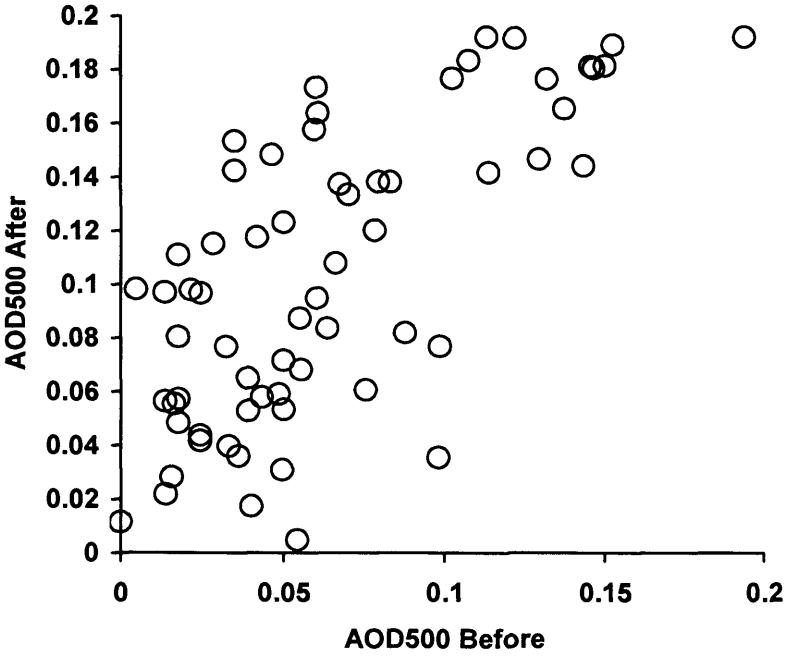


Figure 41. AOD500 changes before (x-axis) and after (Y-axis) laser iridotomy.

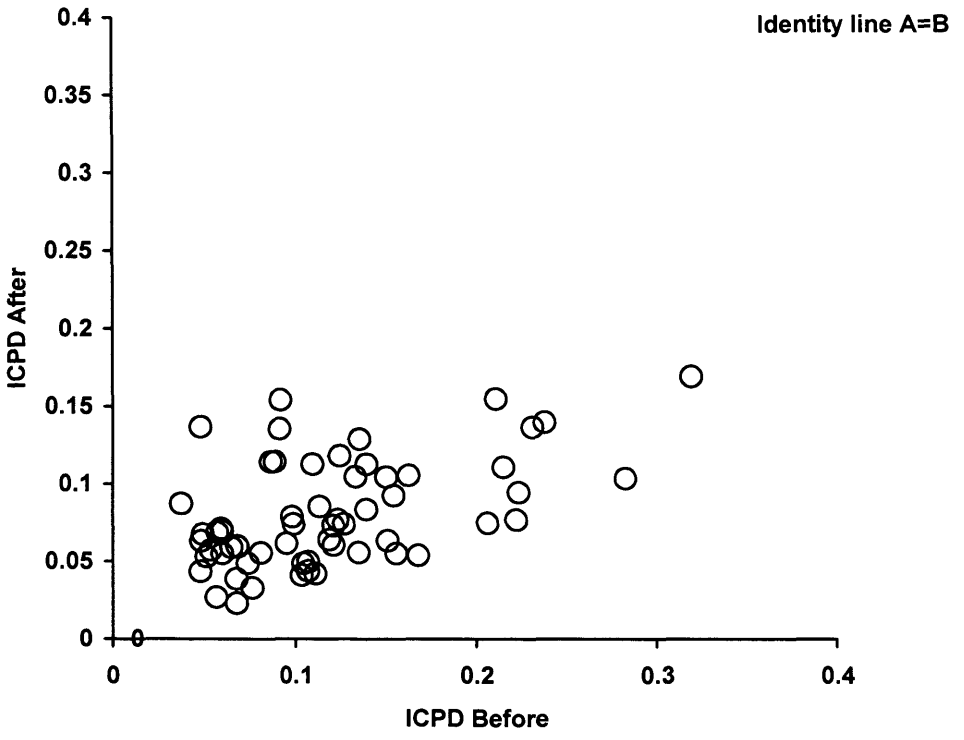
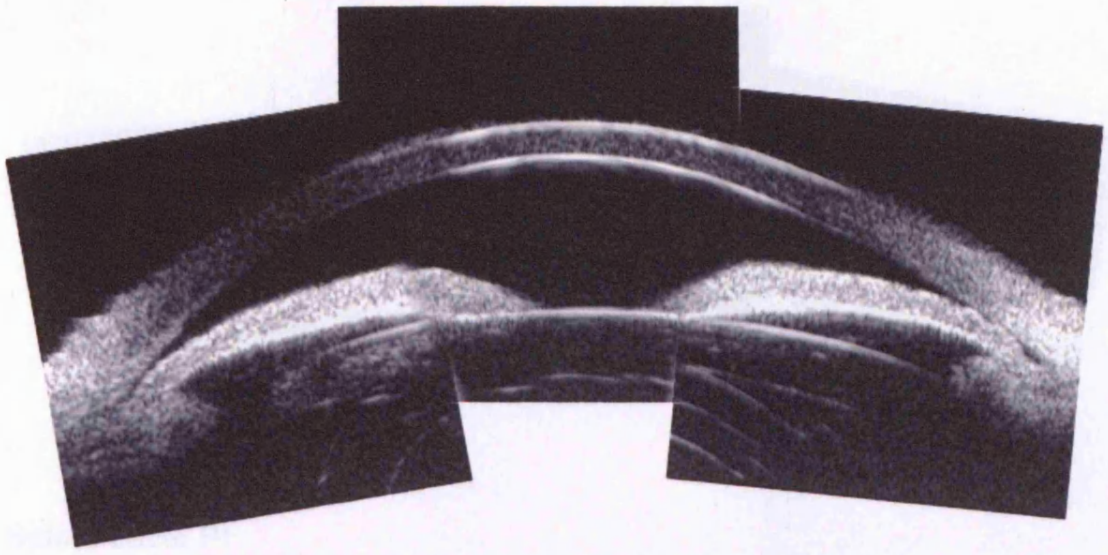
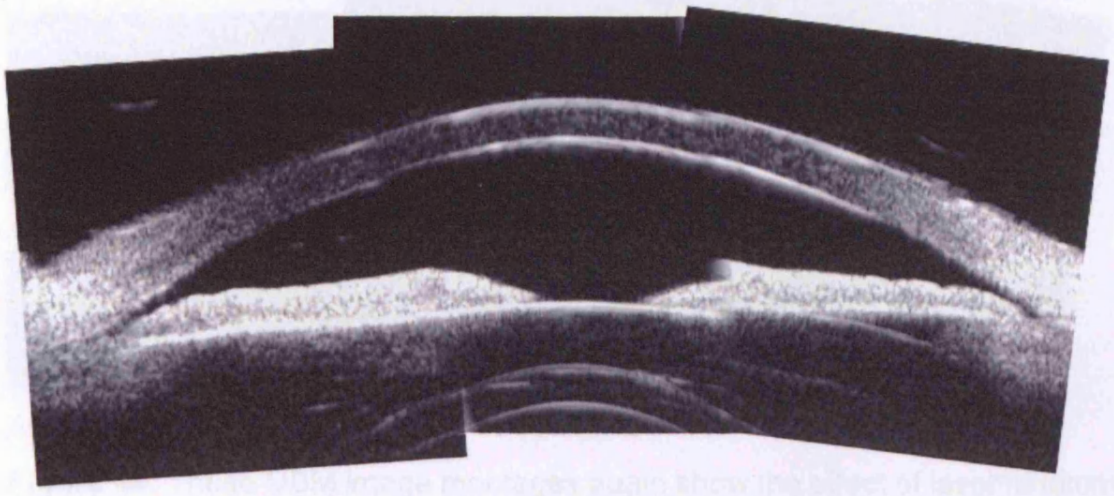


Figure 42. Irido-ciliary process distance before (x-axis) and after (y-axis) laser iridotomy

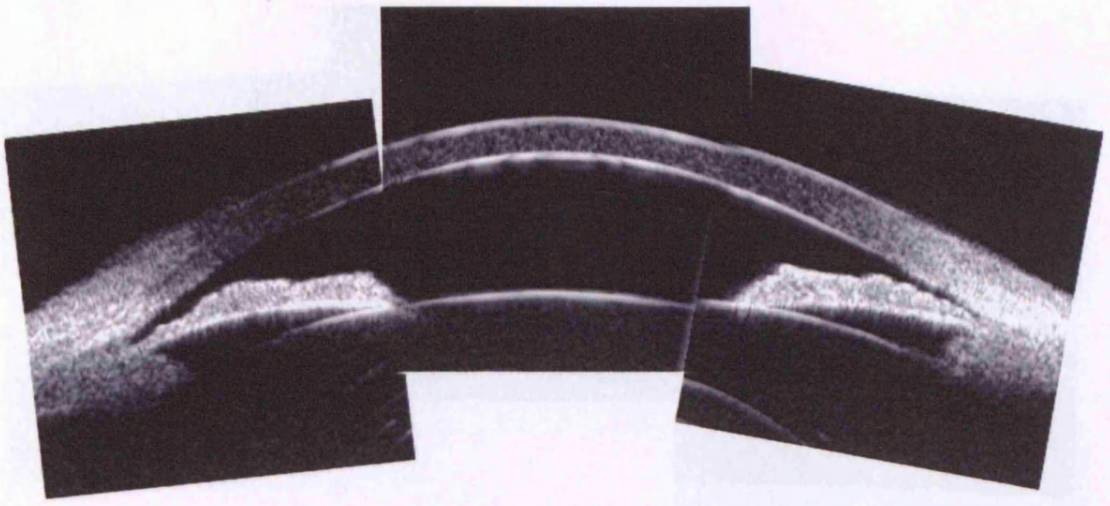


Before Laser PI

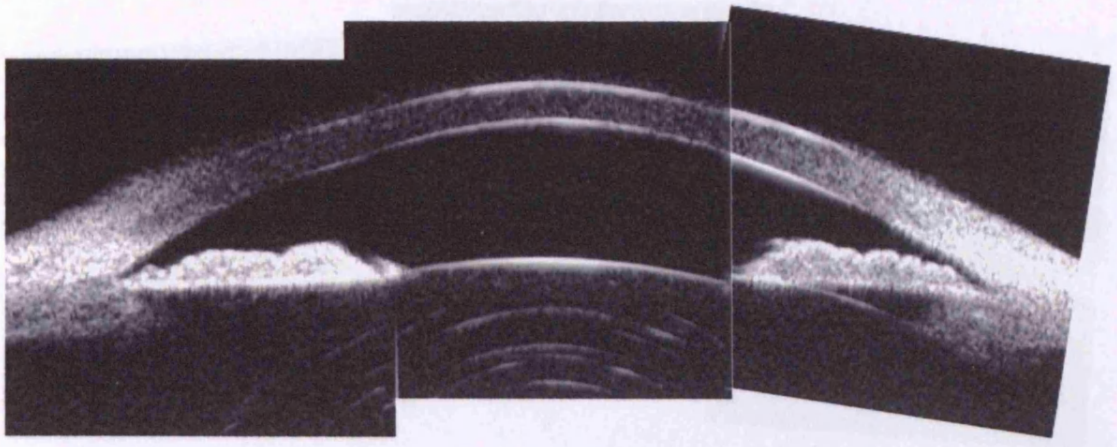


After Laser PI

Figure 43. These two UBM image-montages show the effect of laser iridotomy. The angle is opened after LPI: iris contour becomes flat. The iris insertion is near the middle of ciliary body, and the ciliary body is anteriorly-rotated.

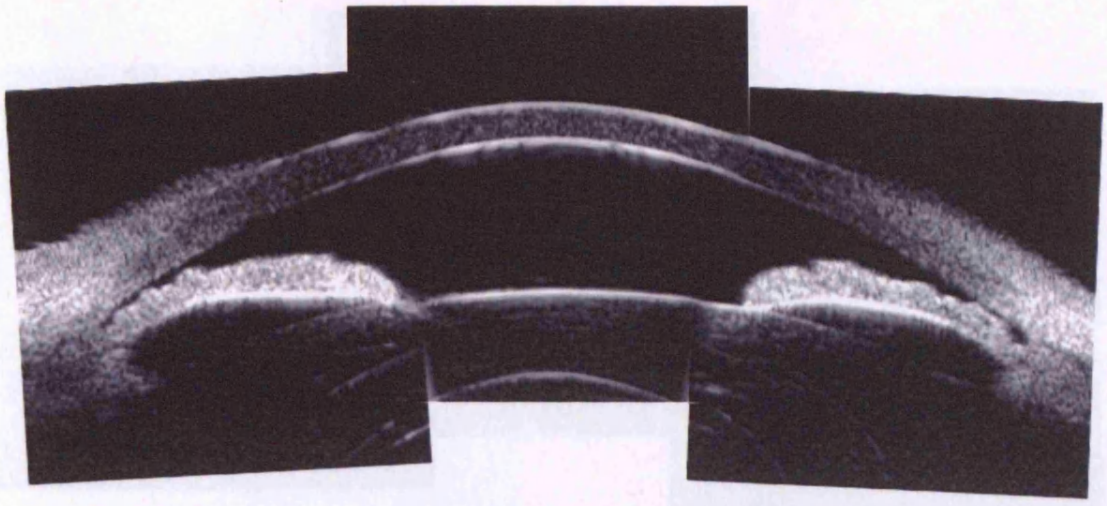


Before Laser PI

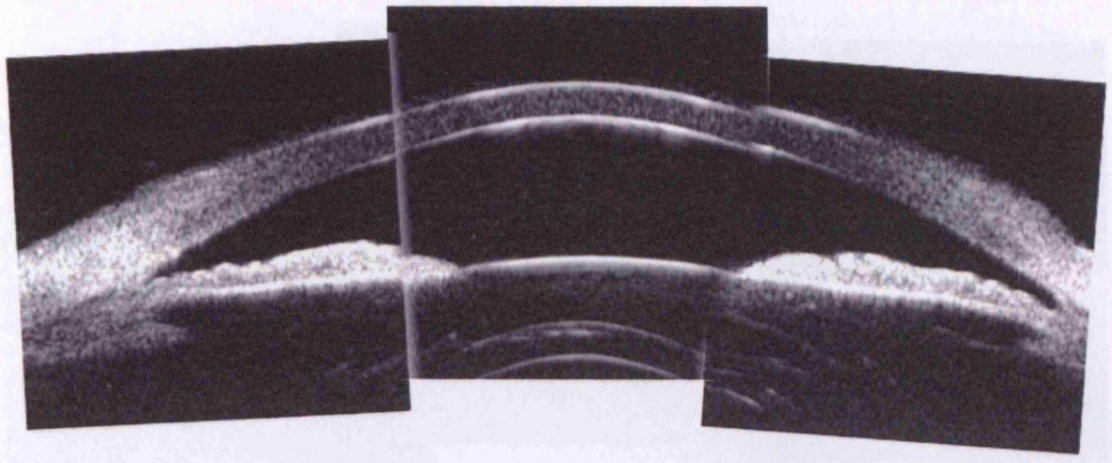


After Laser PI

Figure 44. These UBM image montages again show the effect of laser iridotomy. Angles are opened after Laser PI. The iris iris root is thin at its point of insertion although the ciliary body is anteriorly rotated on superior quadrant (right).

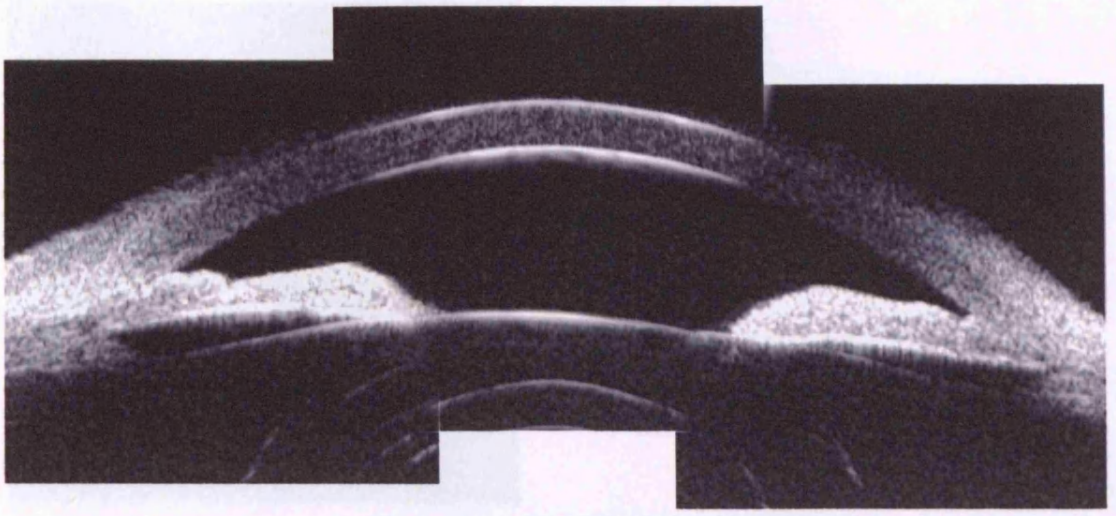


Before Laser PI

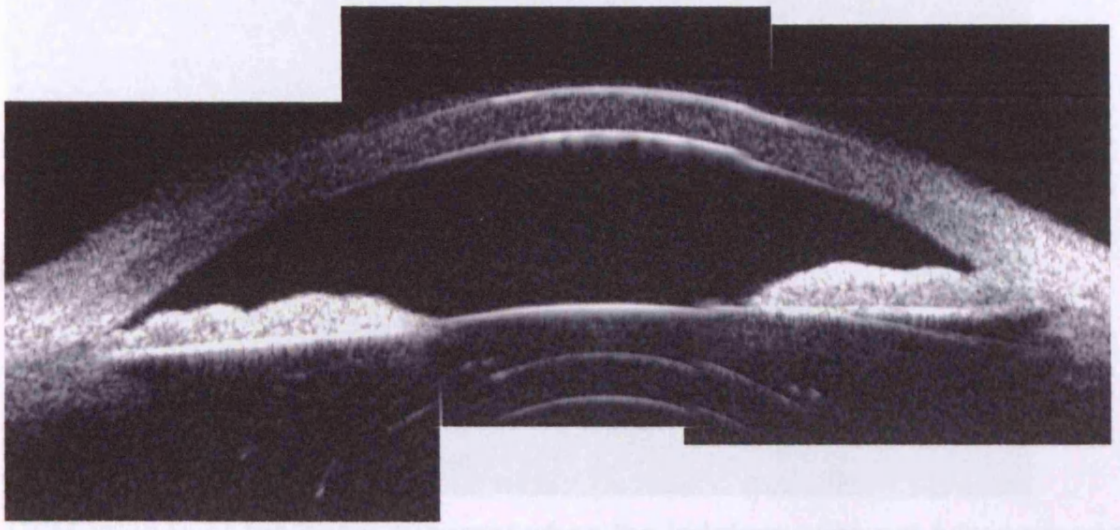


After Laser PI

Figure 45. This UBM image-montage shows the effect of laser iridotomy. Angles have opened after laser PI, and the iris plane becomes flat. The iris insertion is into the middle of the anterior face of the ciliary body, suggesting the location of iris insertion is important.

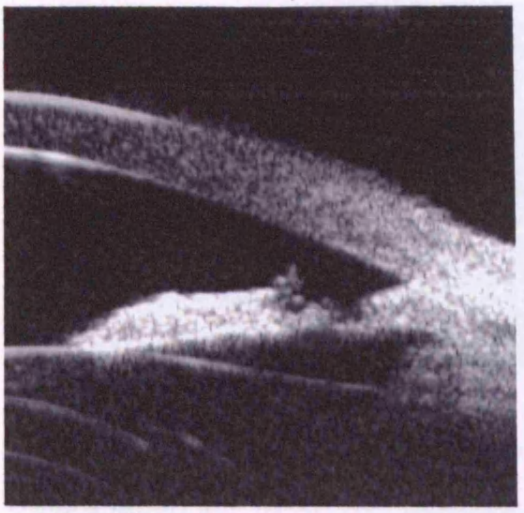


Before Laser PI

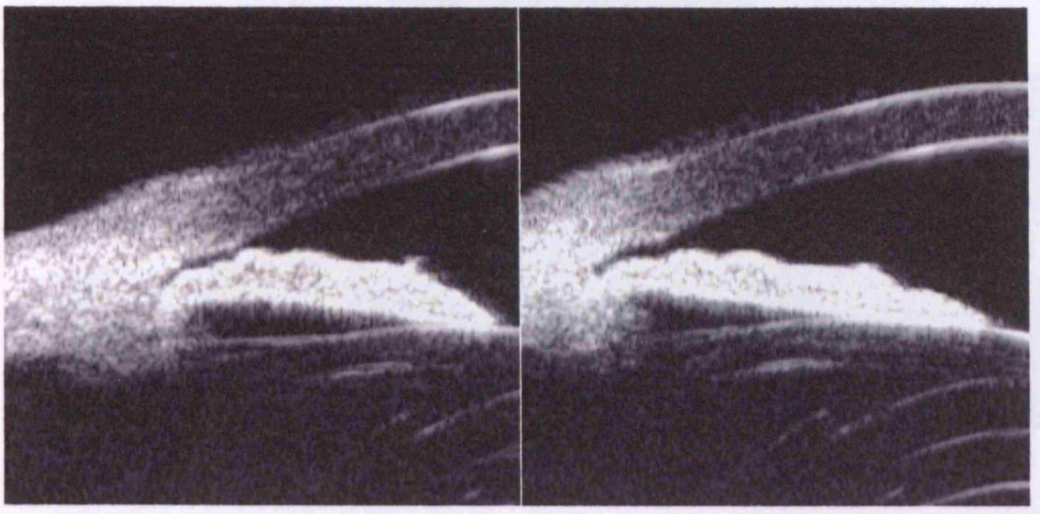


After Laser PI

Figure 46. This UBM image montage illustrates the effect of laser PI on angle configuration, And shows that the superior angle (right) has not opened because of PAS, while appositional closure in the inferior quadrant has been eradicated after laser PI.

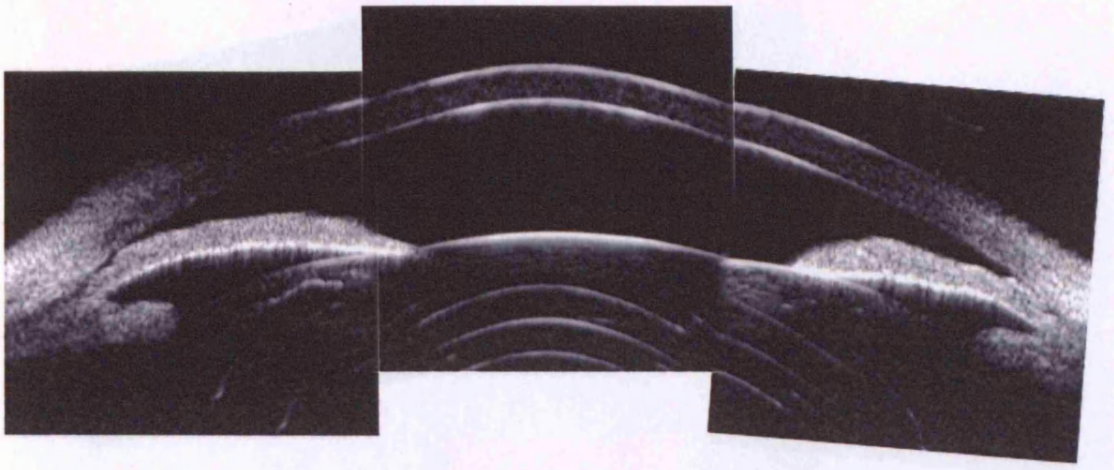


A UBM image showing an attempted iridotomy not fully perforated



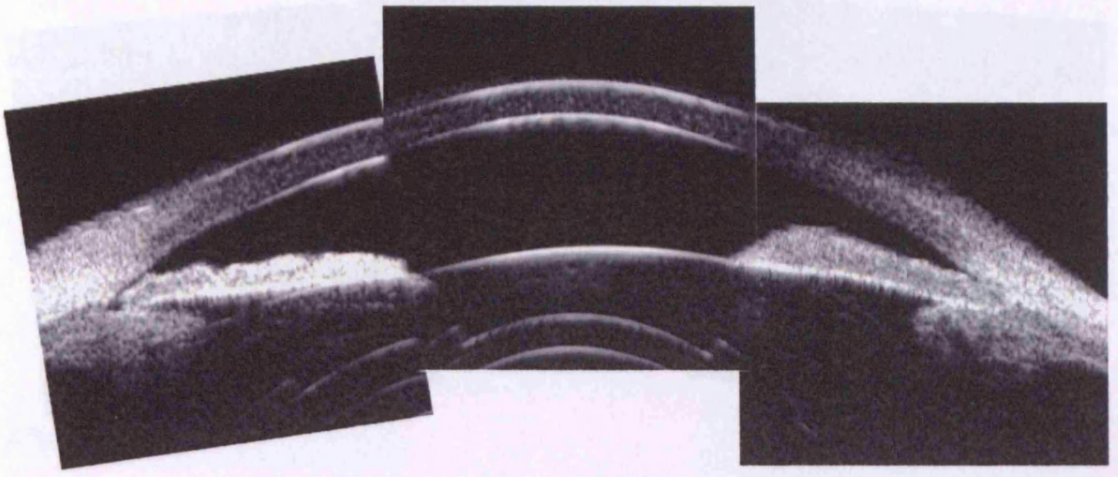
UBM images of the nasal quadrant when the iridotomy was not fully perforated (left), and after successful completion of the laser iridotomy (right)

Figure 47. UBM images on superior quadrant demonstrating that the iridotomy is not perforated. The effect on iris flattening is shown on the lower two images. These figures suggest that we have to make sure the patency of iridotomy at first when studying the efficacy of laser PI.



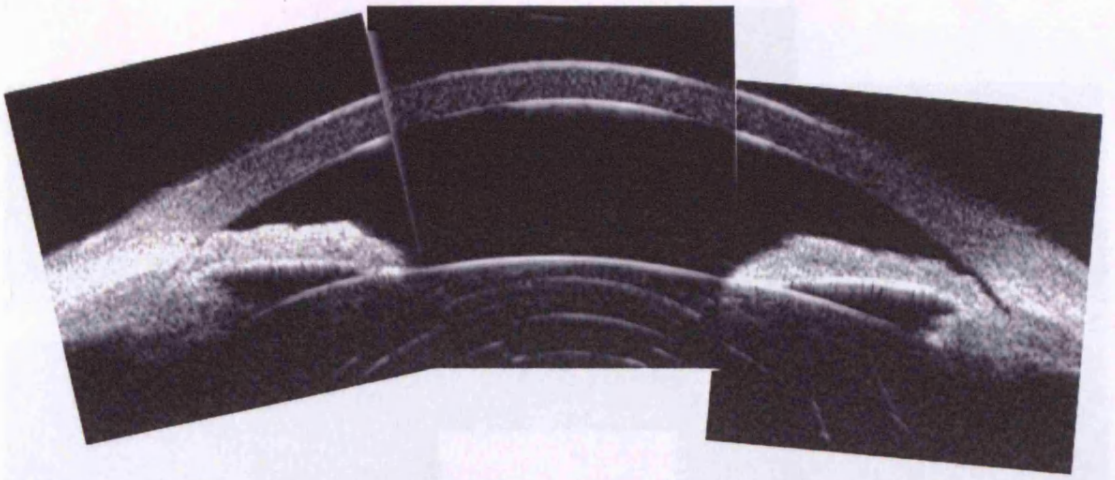
(

Before laserPI

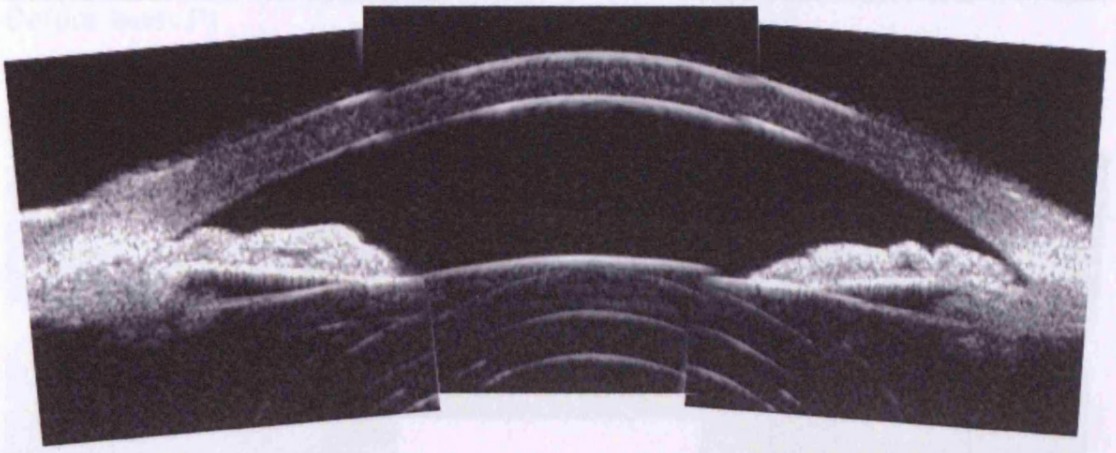


(After laser PI)

Figure 48. UBM montages showing the characteristics of an eye with an angle that remains closed after LPI. The ciliary processes are horizontally-orientated, there is an anterior iris insertion, but iris is not particularly thick. (Left: inferior quadrant; Right: superior quadrant)

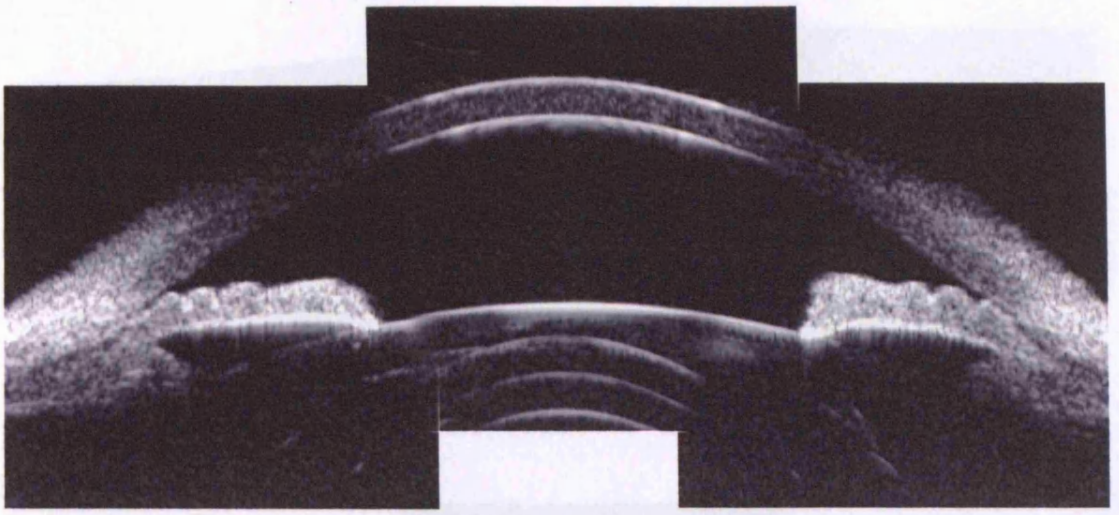


Before laser PI

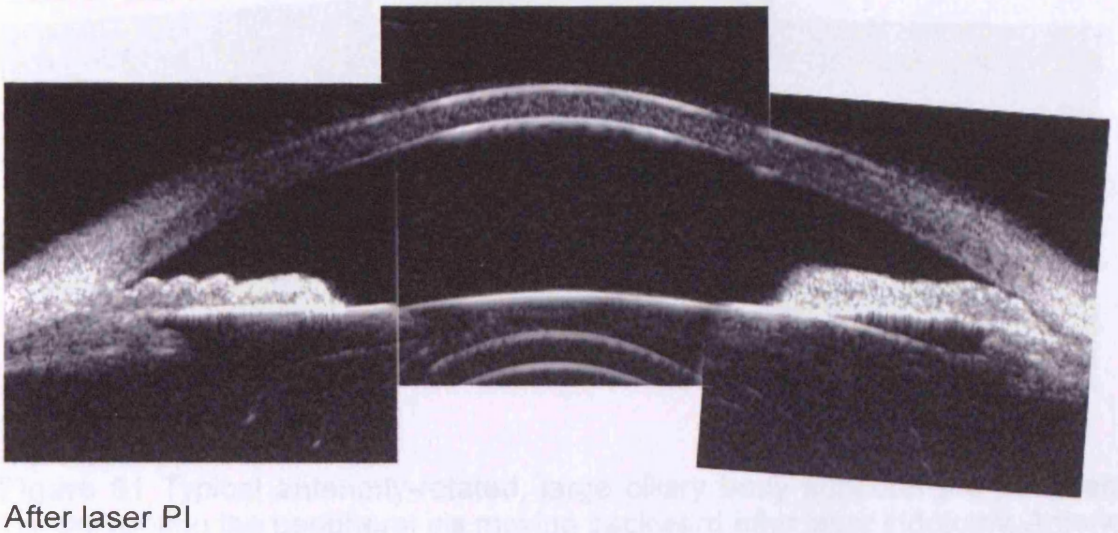


After laser PI

Figure 49. A UBM image montage illustrating characteristics of an eye with residual angle-closure after laser iridotomy in nasal (left) and temporal (right) quadrants. The iris is thick and has an angulated insertion that is also anteriorly-located in nasal quadrant. Anterior rotation of ciliary body is present but does not contribute to the closure because there was patent iridociliary sulcus between the back of iris and ciliary process.

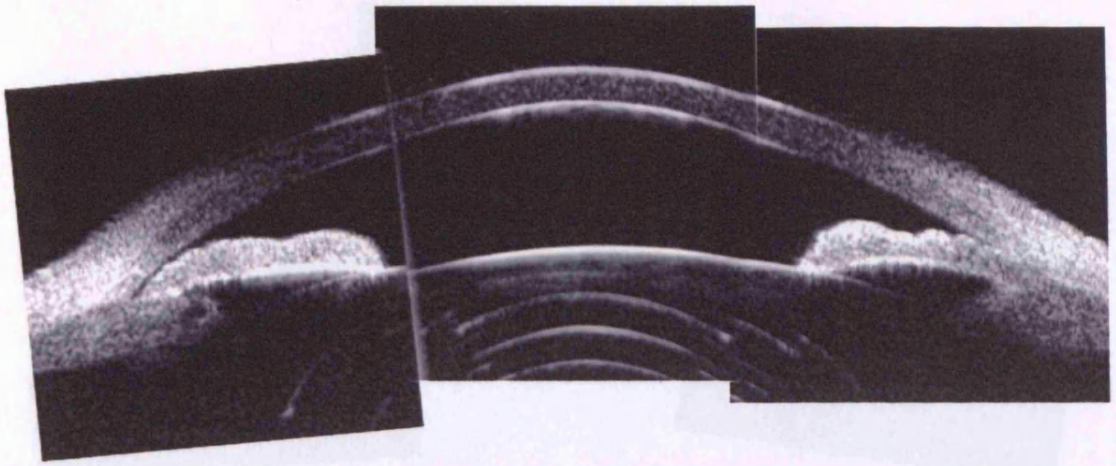


Before laser PI

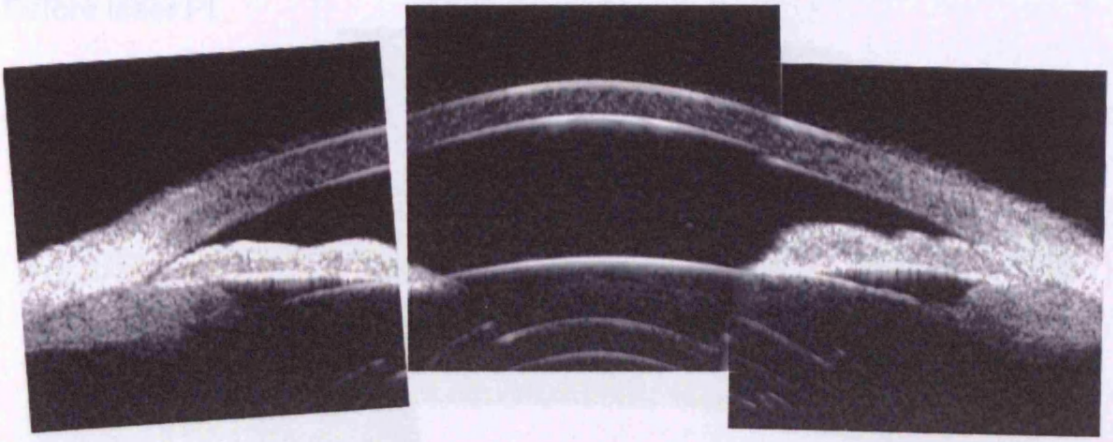


After laser PI

Figure 50. Characteristics of eyes with residual angle-closure after laser iridotomy. There is an anteriorly-rotated ciliary body and thick peripheral iris in the superior quadrant.

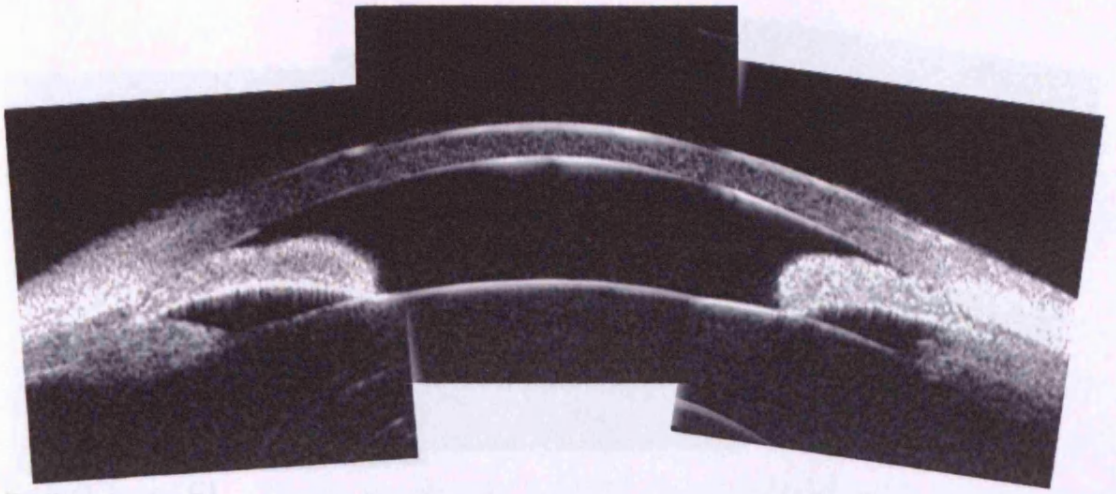


Before laser PI

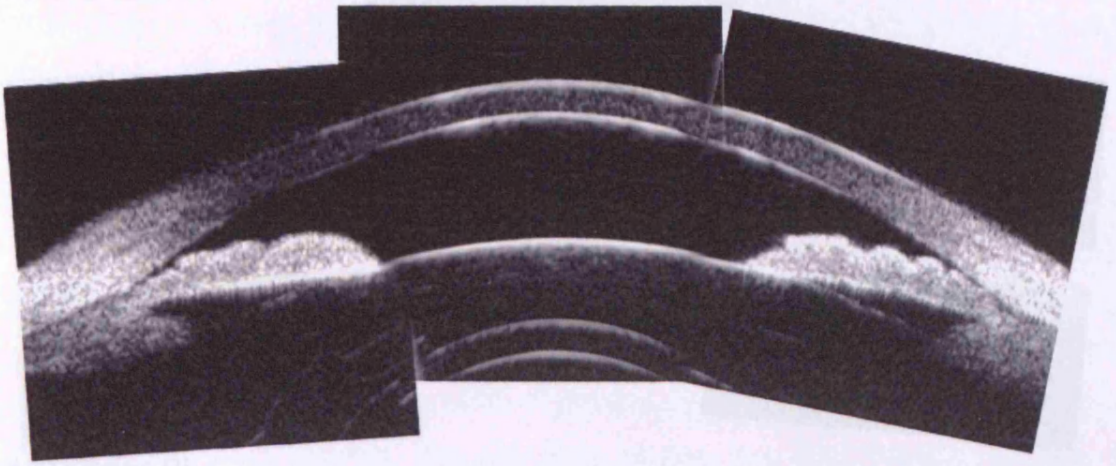


After laser PI

Figure 51 Typical anteriorly-rotated, large ciliary body supports the peripheral iris, preventing the peripheral iris moving backward after laser iridotomy. Anterior location of the iris insertion also plays a role in this mechanism.



Before laser PI



After laser PI

Figure 52 A UBM image montage illustrating the characteristics of an eye with residual angle-closure after laser iridotomy. There is a thin, basal iris insertion. However, the iris remains relatively thick close to the TM. The iris insertion is anterior, and the axial anterior chamber is very shallow. The ciliary processes have a horizontal orientation, and anterior rotation is not present (the iridociliary sulcus is wide open).

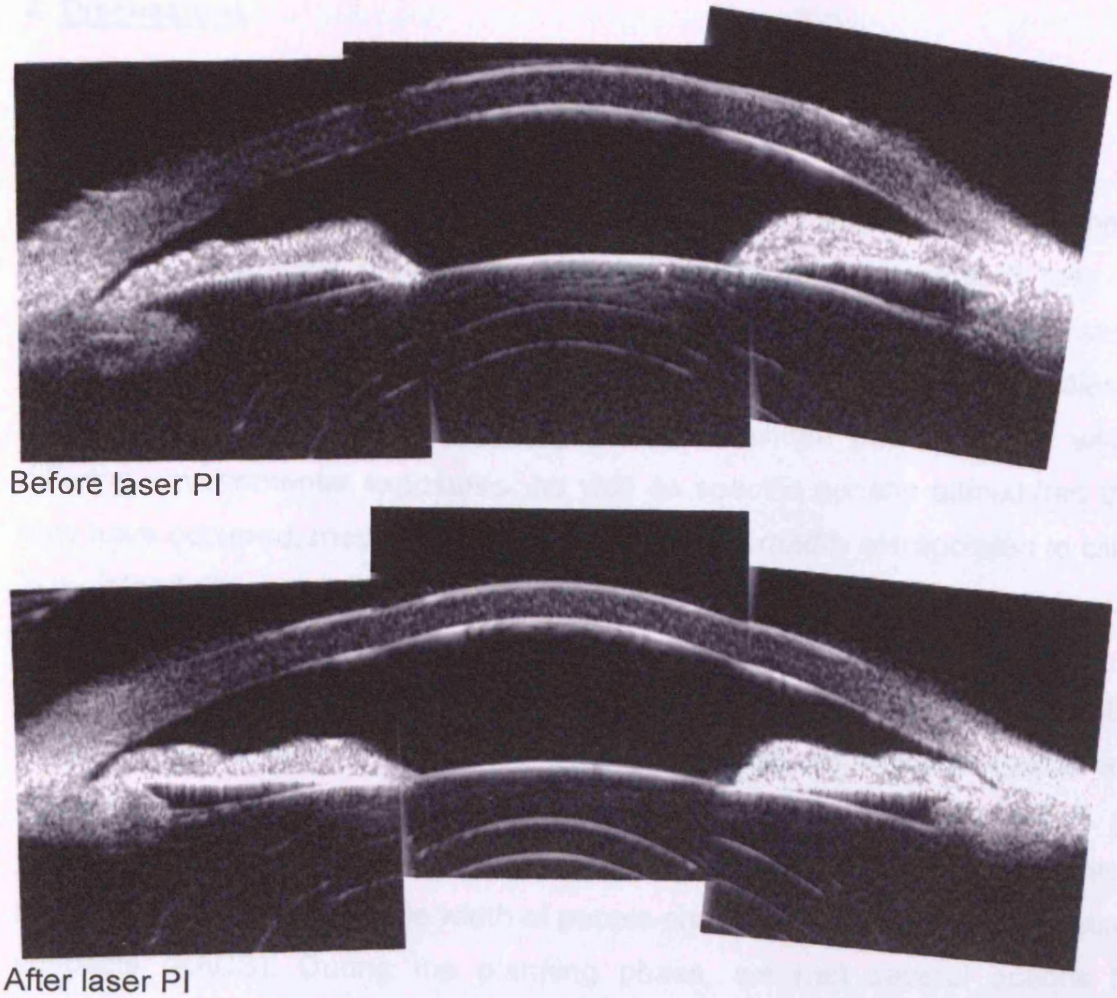


Figure 53 A UBM image montage showing an eye with an angulated iris insertion in the inferior quadrant (left). There is a large ciliary body that is anteriorly-rotated, although the irido-ciliary sulcus appears wide open.

4. Discussions

4.1 Prevalence survey of adult Chinese population

This study, is one of a very limited number of population studies of adult Chinese, specifically examining prevalence and risk factors for glaucoma. It may be unique in that it was conducted in an urban setting in mainland China. Hu's study in 1989 targeted a rural population in Shunyi County near Beijing.[21] Studies in Singapore[28] and Taiwan[7] dealt with overseas Chinese populations in which differing environmental exposures, as well as specific genetic admixtures that may have occurred, meaning that results cannot be readily extrapolated to cities in mainland China.

The primary aim of this study was to describe the biometric characteristics related to angle-closure in Chinese eyes, using both conventional optical and ultrasound biometry, as well as ultrasound biomicroscopic biometry (UBM). An important additional aim was to investigate the short term effect of laser peripheral iridotomy on angle width of people classified as primary angle-closure suspects (PACS). During the planning phase, we had several options for enrolment of subjects: firstly, hospital-based patients; second, enrolling people from a specific sector of the community, such as university retirees who live in a government-maintained residential compound. Both these options would be pragmatic solutions to the problems of limited time and resources. The enrollment of subjects from hospital clinics would probably lead to selection bias. Additionally, patients in hospital clinics tend to present because they are aware of specific symptoms. They may also be less willing to participate because they are mainly fee-paying patients, and consequently expect a high standard of clinical care while tolerating very little inconvenience as a consequence of participating in research project. This situation is true particularly in the hospital where the recruitment would have been carried out, if this option were chosen.

4.1.1 Sampling and subjects

After conducting a pilot study in a university retirees club in Guangzhou during 2002, it seems that retired university staff may have been a viable study cohort. We considered recruiting a cohort mainly composed of academics and

professionals, as well as other grades of staff who had retired from Sun Yat-Sen University, to which Zhongshan Ophthalmic Centre is affiliated. However, this group of people was not likely to be fully representative of the general population of Guangzhou. Because the residents of this area are mainly university academic, and tend to be more educated, and probably have a higher prevalence of myopia and better access to health care services, again the degree to which they are representative of the general population must be questioned. In addition, most of them have busy social lives that may make scheduling examinations and follow-up difficult. In fact, in June 2003, when we approached the administrative staff responsible for the retirees at the university, we were informed most of the retirees would be away on holidays during autumn of 2003, at the time we were planning to conduct this study. Accordingly, we felt it necessary to draw a sample of subjects from the general population, while being aware that recruiting and examining a community-based sample would be more difficult and costly. We were fortunate to receive the full support of the local government when we explained our aims and objectives to the Governor of the City in Guangzhou. The local government administrative staff were asked to work on this project on a volunteer basis, because the government made this project one of their health care objectives for 2003. Shortly after the approval from the government, we successfully obtained equipment from the University Department of Preventive Ophthalmology and recruited a group of doctors and nurses.

Liwan District is an "old district" of Guangzhou with limited recent urban development. It was selected as the location for this project mainly because of its relatively stable population and strong community programs. Most residents living in this area were born there or have lived in the area for a long time. It is believed that many have lived in the same old house for several generations. Liwan district has a population of 515,000 people living in an area of 6 square km, and has a complicated network of streets, lanes and alleyways. To draw a representative sample of subjects using random sampling of the population, and to be able to examine them, we knew would be very challenging. We estimated that about 300 subjects would need to be examined up to three times, in order to ascertain their visual field status, to perform laser iridotomy and to complete UBM examination pre- and post-laser. Also, we intended to conduct further

examinations on subjects at a later date, aiming to study long-term outcomes in those treated, and identify incident disease in those who were untreated. In order to maximize response rates, and as a consequence of relatively limited resources available, we decided to select just 1 of 12 administrative "street block" units as the sampling frame. Fengyuan street block was selected for convenience because of its strong community administration; it was honored by the government as the "Model Street" for government immunization program. This street block had a population of 62,815 people, 13,942 of them being aged 50 years and over in 2003 according to the National Census data in 2000. Clustered, random sampling (using the Resident Registry list) was then used to identify subjects aged 50 years and over in this street block. The sample size needed for this study was estimated at 1,500, assuming prevalence of glaucoma was 3%, and accepting a sampling error of 20% of prevalence.

Detailed personal information in the census database is classified as confidential by the government and requires a complicated application process if the information is to be released for public use. Therefore, the Resident Registry was used as the sampling frame, from which eligible subjects were identified. Registration is a legal requirement. The register is kept in the police station and details all permanent residents in the city. This dataset is updated on a yearly basis, assimilating information on migration, death and new births. Using this information to identify households with eligible subjects, the need to perform door-to-door enumeration of all households in the area was avoided. The demographic characteristics of the sample drawn from the registry were compared with that in Fengyuan Street Block (sampling frame) and Liwan District. Except for people in their 60s being under-representative by around5%, the age and gender distribution of participants, the sampling frame and district were broadly similar.

Community workers accompanied by research investigators then went door-to-door visiting the households identified as having eligible subjects. Invitation, recruitment and informed consent were all administered during this visit. We discovered that 430 people had been moved out of the area prior to a major road construction project, and in some cases that a household was not occupied by registered resident. These people who were not verifiable as being

resident in the study area were distributed evenly throughout each age group. As a criterion for enrollment, we specified that subjects should have lived in the area for more than 6 months. People who had moved from the area were no longer considered eligible subjects, but those whom were still resident (confirmed by the neighbours and community workers),, but could not be contacted during 3 door-to-door visits were still considered eligible. By using these criteria, older people who had moved into institutional care were not included in the study. Some of those may have been blind and therefore their omission from the study will have affected our results. During the enumeration process, we were not able to quantify or characterize this group of people moving to institutional care homes.

The overall response rate in this study was 75.3%. Younger men (aged 50-59 years) had a disproportionately lower response rate (63.6%) than others. Being still of working age and having no time attend for examination were the major reasons given for non-attendance. Lower response rates were also encountered among elderly people (aged 80 years), possibly reflecting their limited mobility and poorer physical health. After becoming aware of the difficulty in recruitment of younger subjects, a weekend clinic was set up and the daily schedule for examinations was extended up to 6pm. Home visit were not undertaken extensively as many people were not comfortable to have doctors visit and examine family members at home. Efforts were also made to visit non-responders in order to explain the purpose of the research and encourage them to them to participate. We also asked subjects who had already been examined to visit non-responders and act as motivators during these home visits. It is acknowledged that having a sizeable number of absentees in younger age ranges may have distorted the data concerning the distribution and impact of various anterior segment biometric characteristics. Absenteeism in those aged 80 years may have less influence because their proportion in the population is low, although the proportion of those affected by disease will be correspondingly higher.

4.1.2 Examination and diagnostic criteria

The definitional criterion developed by ISGEO was used in the current field study [9]. Because definitive information on the presence of glaucomatous disc and field

damage is not always available in field studies, the identification of glaucoma can be made on 3 levels of evidence. The highest level of evidence requires optic disc and visual field evidences (VCDR or asymmetry $\geq$ 97.5th percentile and reproducible glaucomatous field defect). In the second, if the visual field test could not be performed satisfactorily, a severely damaged disc (VCDR or asymmetry $\geq$ 99.5th percentile) is considered compatible with glaucoma. The 3rd level of evidence specifies that if the optic discs cannot be examined due to severe media opacity, subjects who are blind (visual acuity < 3/60) and have undergone previous glaucoma surgery, or have an IOP greater than 99.5th percentile may be diagnosed as suffering glaucoma. The division of cases of glaucoma into PACG and POAG is based on the gonioscopic finding of an occludable angle (where the posterior, usually pigmented, trabecular meshwork is not visible for 270 degrees or more during a static examination) or a reliable medical history, if the angle status has been changed by previous treatment. The elevated IOP and PAS formation are not considered prerequisite in the diagnosis for PACG.

There were several important issues relating to this classification scheme that should be emphasized. The vertical cup:disc ratio is the cornerstone of the ISGEO diagnostic scheme. A definite case of glaucoma should have an enlarged VCDR, or one that is asymmetrical with the fellow eye. Those with glaucomatous field damage but having a VCDR below the diagnostic threshold, probably as a consequence of a small optic disc, will have been mis-classified. Crowston examined and confirmed the impact of variation in disc size on VCDR in the population of Blue Mountain.[157] Furthermore, the identification of the cup margin may be difficult in some cases, particularly in myopic eyes or discs with a flat contour.[158] This feature is common in Chinese eyes. All of these factors may perhaps compromise the accuracy of the figures for prevalence of glaucoma, and consequently, the estimates presented here are conservative.

Visual field testing of all subjects may be the only solution in trying to avoid these problems. If field testing has to be performed on all subjects, it should ideally be conducted at the beginning of the examination, so that disturbances to the cornea and bleaching of the retina during the fundus examination can be minimized. Indiscriminant psychophysical testing will be time-consuming and

potentially affect the attendance rate, let alone a significant number of seniors cannot co-operate visual field test. Also, a large number of patients with suspected field defects will need to return for repeat, confirmatory testing. At the end of the examination, even with successful repeated field tests, about 60% of those with reproducible field defects compatible with glaucoma, but having normal discs will require further, more sophisticated examinations, perhaps not available in the field, to exclude the other abnormalities.[9] These difficulties all make this option impractical in all except the most well-resourced settings.

As it had been decided from the outset to use the ISGEO diagnostic scheme, visual field testing of all subjects was not performed. Only when subjects were found to have suspected glaucomatous disc damage or elevated IOP was field testing performed. In order to avoid any adverse effect of previous corneal and retinal examination, field testing was performed on a separate day, and repeated if the first test showed unsatisfactory reliability indices or a field defect compatible with glaucoma.

Assessment of the cup:disc ratio in the current study was performed during a slit-lamp examination while using a +78D lens. In most cases this allows a stereoscopic view of the disc (stereoscopic views make the assessment of the margin of cup and disc easier). However, the disc assessment was not routinely performed with pupil dilation. The pupil was dilated only when the disc could not be seen satisfactorily. The cup:disc ratio assessment may therefore have been underestimated in eyes with small, undilated pupils. Kirwan et al [159] have described that pharmacological mydriasis of the pupil improves the inter-observer agreement in calculation of the vertical cup:disc ratio. The decision on not dilating pupil for everybody is also because of the dilation of the pupil will potentially induce acute episode in some people with narrow angle, possibly adversely affecting the vision of the subjects and for further recruitment.

In order to improve the objectivity of the cup:disc ratio assessment, a set of standard photos of VCDR grades was used. Stereo fundus photography was performed in the subjects with either uncertain or suspected glaucomatous optic neuropathy (based on measurements of VCDR) for the purpose of verification of diagnosis. Emerging techniques, such as confocal scanning laser

ophthalmoscopy (using the Heidelberg Retina Tomograph) may offer more reproducible assessment.[160;161] Unfortunately, this was not feasible in the current study.

Gonioscopy was the primary outcome measure in the study of prevalence of angle-closure. The examination and classification was performed according to a standard protocol (see Methods section). In brief, the angle width was graded using the Shaffer scheme. The apparent and true level of iris insertion, and iris profile were scored using the Spaeth grading scheme[162]. In iris profile assessment, a category of "plateau" was added, as used in previous surveys [24]. The circumferential extent and height of PAS was recorded on a goniogram. The "biometric gonioscopy" method suggested by Congdon et al[54] was not used because it is particularly difficult in eyes with narrow angles. This examination method requires the use of a slit lamp eyepiece measuring graticule to measure the distance between iris insertion and Schwalbe's line on static and dynamic gonioscopy. Validation studies suggest this technique is highly correlated with Spaeth gonioscopic grading of angle width and iris insertion, and has potential for good inter-observer and intra-observer agreement[54].

The gonioscopic examination techniques used in the current study were subjected to studies of inter-observer agreement between myself and Dr Foster during his field visit to Guangzhou. The weighted Kappa values for Shaffer angle width were 0.62~0.63, indicating good agreement. Better Kappa values were on apparent iris insertion grading, ranged from 0.67 to 0.84 (good to excellent agreement). The grading by Dr Foster was generally narrower but this difference was not statistically significant using a paired t test. Because of the limited time available for testing of agreement, the subjects in this series had mainly wide angle, meaning the number of cases available to measure agreement in differentiating occludable angles was insufficient. However, the level of agreement on angle width is compatible to the study in Mongolia [8;163], but inferior to that reported by Spaeth group[53].

Gonioscopy examination itself is highly subjective. Similar to the Shaffer angle grading system, the Spaeth scheme defines the width of angle as the geometric angle between the tangent to the surface of the trabecular meshwork and the

tangent to the surface of the peripheral third of the iris. This estimate is subjective and will inevitably vary between different examiners. Similar difficulties exist in specifying the apparent iris insertion. In this study, the data suggests the agreement of grades of apparent iris insertion in least in the superior quadrant (Wt. Kappa: 0.69) and best in the inferior quadrant (Wt. Kappa 0.84). Therefore, gonioscopic examination by the same examiner throughout the whole course of the study probably benefits the consistency and reliability of the results. Using objective criteria, with methods of standardization such as photographic standard images, probably enhances clinical grading in research. Another advantage in this study is that the gonioscopy was performed before the optical and ultrasound pachymetry so that the examiner was masked to these "supporting" evidences. The observer bias, to some extent, could be minimized.

Intraocular pressure was measured in all subjects as the first step in the examination process. In this way, it was intended to minimize the effect of the other examinations on IOP. Tonopen alone was used for this measurement.[164] This decision was taken in light of results from a manometric study of IOP measurement error in Singaporean people, which suggested that Tonopen offered a small but significant benefit in terms of better accuracy than applanation tonometry (using a Perkins Tonometer).[165] In this study, the level of IOP was set to between 10~30mmHg. The mean measurement error was significantly less for the Tonopen (-2 mmHg relative to manometric IOP, range: -8 to +4mmHg) than for the Perkins (-4 mmHg relative to manometry, range: -11 to +3 mmHg). This study found that measurement error was associated with the level of IOP, and that the magnitude of the error was higher in eyes with higher IOP. Given that Tonopen is often quicker, and was well-tolerated by our subjects, it was used as the only method of IOP measurement in this study.

Population data from Dutch, Singaporean and Mongolian people suggest the IOP is positively correlated with central corneal thickness (CCT), with IOP increasing by 0.19 mmHg per 10 μm increase in CCT.[166;167] This association, although relatively small in magnitude, may make the comparison of IOP between different populations difficult if the distribution and variation of corneal thickness also differ.

Validation of the UBM image acquisition and analysis is discussed below.

4.1.3 Prevalence of glaucoma

Using the definition of glaucoma described above, and in the method section, emphasizing glaucomatous optic neuropathy, a total of 53 individuals were identified as glaucoma cases. Among them, half of the cases were diagnosed on the basis of abnormal VCDR combined with a reproducible field defect (category 1, 28 cases), 1/3 of the cases by only VCDR when visual field testing was not possible (category 2, 17 cases), and 15% identified on the basis of previous history of glaucoma surgery (usually trabeculectomy) or significantly elevated IOP and severe visual impairment (category 3, 8 cases).

The category 1 definition used in the current study required that visual field defects be proven on repeated visual field testing. Incomplete testing would therefore bias the results toward an under-estimation of prevalent glaucoma. In our study, about 1/2 of glaucoma cases were confirmed by identifying reproducible field defects and combined with a statistical abnormality of VCDR indicating probable structural damage. The other 42 of 183 subjects who had a VCDR compatible with a diagnosis of glaucoma could not cooperate to complete visual field test or did have glaucomatous field defect but not able to show up for the repeated field test--among them, about 1/5 (9/42 cases) were diagnosed as glaucoma based on category 2 or 3 criteria. About a third of the 42 cases were very elderly, and frequently had significant media opacities. A few glaucoma cases may have been missed in this group of patients.

Table 53 compares the age-specific prevalence of all glaucoma in Baltimore whites, Baltimore blacks[19], Barbados blacks[168] and the data from East Asians populations in Japan[23], Singapore[24], Mongolia[8], Thailand[169] and the current study in urban Guangzhou. The census data from the year 2000 in Liwan District, Guangzhou is used as standard population. The age and sex standardized prevalence in Guangzhou is lower than in all East Asians populations and the African populations, but higher than in people of European origin. The age standardized prevalence in men is about 1.5~2 times higher than in women. This has been a consistent finding in Mongolia, Singapore, Barbados, Baltimore

blacks. A higher prevalence in women was found only in Thailand, Japan and the white population of Baltimore. Examining the age-specific prevalence rates, an increase with age was observed in almost all studies. The prevalence figures in the 50-59 and 60-69 years in Guangzhou are similar to what has been found in other East Asian population. However, the prevalence in 7th decade is lower, and this may in part account for the lower standardized prevalence in Guangzhou.

One has to be cautious that this comparison may be subject to potential errors; the diagnostic criteria are not uniform across different studies. Although the studies in Mongolia, Singapore and Guangzhou used similar diagnostic "scheme", some methods, in particular those used for field testing, do differ somewhat. The studies in Mongolia, Singapore and Thailand used a Henson field analyzer (it was also used as an initial screening method in Singapore). A Humphrey Field Analyzer was used as the method of definitive field examination throughout in both Singapore and Guangzhou. Also, the definition of a field defect compatible with glaucoma was identical in Singapore and Guangzhou, but differed from that used in the other studies. In addition, the criteria used to decide who should undergo full threshold visual field test were different in these two studies: in Singapore, threshold field testing was performed where subjects failed to produce a normal test on screening (Henson or FDT), had raised IOP, a narrow angle on gonioscopy or a suspect optic disc. In Guangzhou, field testing was only performed in subjects with suspected structural damage to the disc and/or elevated IOP. The methods for assessing disc damage were also different: in Guangzhou, the VCDR was assessed at a slit lamp using a +90D lens without dilation of the pupil. Dilation was performed only when media opacities did not allow a clear view of the fundus (in Singapore all subjects had their pupils dilated). In all eyes where the disc was felt to potentially glaucomatous, stereo photographs were taken as a confirmatory measure. Consequently, the specificity of diagnosis in the current study should be high, although the sensitivity will probably have been compromised.

The prevalence and importance of POAG in Chinese populations remains one of the major issues both on a practical level in Chinese societies, and as a scientific issue worldwide. Hu and colleagues [21](1989) reported that the prevalence of PACG in 3,147 subjects aged 40 years and over living in a rural area near

Beijing was 1.4% (44 cases). However, only 1 case with POAG (prevalence 0.03%) was identified. In 1998, Zhao et al working in the same region again found very similar results[173]: PACG 1.66% and POAG 0.29%. The data from Mongolia found that PACG was the predominant form of glaucoma, but the prevalence of POAG was about half that of PACG. In Chinese Singaporeans, POAG was found to be 1.5 times more common than PACG. Similarly, the current study found the prevalence of POAG was 1.4 times higher than PACG. It is intriguing that POAG prevalence was found to be at least 7 times higher than PACG in a Japanese population.[23]

The prevalence of POAG identified in population studies depends on a number of factors. The examination methodology and diagnostic definitions are major determinants of the prevalence. Wolfs et al demonstrated that when various definitions were used, the prevalence of POAG varied between 0.1% to 1.4% in younger members of the cohort to between 0.9% and 5.9% in older people.[170] When looking at the previous surveys conducted in mainland China, in the study in rural Shunyi county, near Beijing,[21] POAG was defined as elevated IOP at three occasions (at the same time of three different days) with three positive or two "strongly positive" results in three subsequent tests: glaucomatous disc damage, glaucomatous field damage and drinking water test, although the definition of either "positive" or "strong positive" was not clearly described. The use of elevated IOP as a defining characteristic of glaucoma is not compatible to the current understanding of the POAG, as IOP is no longer considered a defining feature of the disease. Hence, disc and field assessment may not have been performed on all subjects. The methods used to assess the disc and field were not described in the publication. A second survey in Shunyi County was primarily designed to investigate blindness, low vision and quality of life assessment.[171] The diagnosis of POAG was mainly based on elevated IOP plus disc assessment by direct ophthalmoscope. As was the case in the first study, gonioscopy was not performed. All these defects in the study methodology will probably have hindered the accurate estimation of glaucoma prevalence (both POAG and PACG) and probably explain in part the low prevalence of POAG. The Mongolia prevalence study used a Henson field analyzer alone as the definitive diagnostic criteria for glaucomatous field loss, which may under-detect the POAG cases at an early stage. The fact that the ISGEO diagnostic scheme

had not been developed at the time of the Mongolia survey means that "category 2" will have been omitted, and this may also underestimate the prevalence of POAG.

Once the GON has been definitively identified, the next step is to classify the patients according to the presumed mechanism- PACG, POAG and secondary glaucoma. The division of cases into POAG and PACG is traditionally made according to the presence of an "occludable" angle by gonioscopic examination, unless the angle structure has been altered by iridotomy, trabeculectomy or cataract surgery procedures. Consequently, the definition of an occludable angle used in the gonioscopic assessment will directly determine the proportions of POAG and PACG. For example, the number of quadrants in which the posterior (usually pigmented) trabecular meshwork is hidden from view has traditionally been set at 3 (i.e. 270 degrees). However, this is not an evidence-based definition. There actually some evidence suggesting that this definition is excessively stringent, and may exclude a large number of people with angle-closure, leading to their mis-classification as POAG.[172;173] It may be that using 1 or 2 quadrants as the defining characteristic is more suitable, although this remains to be further investigated and proven. However, given our current level of understanding, we believe that the mechanism in most PACG cases is obstruction at the pre-trabecular level (peripheral iris obstructing access to trabecular meshwork). We assume that GON due to PACG develops after persistent IOP elevation induced by either appositional closure or damage to the structure and function of the trabecular meshwork (either with or without synechiae). [155] In cases where there has been no medical, surgical or laser treatment, normal tension PACG presumably does not exist. However, in the early and intermediate stages of disease, episodic elevation of IOP will occur, meaning that pressure measurements will not always be elevated.

Table 53 Age sex standardized prevalence of all glaucoma in selected population based studies *

Age Y	Barbados‡‡		Baltimore (B)		Baltimore (W) §		Japan†		Mongolia‡		Singapore		Guangzhou‡	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
N									241	274	432	527	613	792
50	4.7	4	4.6	5	0.7	0.9	2.5	2.8	1.7	1.9	1.7	0.5	1.9	0.4
60	11.2	5.7	9.5	5.7	1.6	2.2	5	4.9	7.4	4.8	5.2	1.8	4.6	1.8
70	20.1	14.7	10	11.5	4.1	3.6	8	8.2	12.5	0	11.5	7.8	5.6	5.4
80	25.8	23.9	23.5	7.5	6.0	3.6	13.1	9.1	0	16.7	0	18.2	21.3	4.9
Age-S	10	6.7	7.2	6.3	1.7	1.9	4.4	4.5	5.9	2.4	4.9	2.6	3.5	2
Age/sex	**8.3**		**6.7**		**1.8**		**4.5**		**4.0**		**3.7**		**2.7**	

* Direct standard population from the Census in Liwan District, Guangzhou in 2000; Only the subjects aged 50 years and over are included in this analysis for each selected study.

§ Additional unpublished data from J.M. Tielsch, PhD 1999

†Additional unpublished data from Y Shiose, MD, 1999

‡Not adjusted for incomplete field data

‡‡Additional unpublished data from M.C. Leske, MD, MPH, 1990

4.1.4 Prevalence of occludable angles, PAC and PACG

The prevalence of occludable angles, PAC and PACG are reported separately in the current study. The diagnosis of individual subjects was made according to the eye with more severe disease if this was different in the two eyes. For instance, for a subject with one eye with an occludable angle, and another eye with PAC, the diagnosis was PAC for the individual.

Population-based data from different countries suggests a variation in the prevalence of PACG, with Europeans at one end of the spectrum and Inuit (Eskimos) at the other. The prevalence of PAC/PACG in European population are arranged from 0.04% in Beaver Dam [16], 0.06% in Melbourne [17], 0.4% in Baltimore whites (JM Tielsch, Personal communication, 1996)[19]. Data from the South Tyrol region of Northern Italy (south European) found a somewhat higher prevalence rate of PACG (0.6%)[20]. In this Italian study, 58% were termed "chronic" PACG, never having suffered an "acute" episode or symptoms. This finding highlights that even in Caucasians, acute episode may not always be the predominant clinical form of PACG. In this study, the diagnosis of PACG required 2 of 3 of the following: glaucomatous disc, visual field loss and IOP >/= 22 mm Hg. It was therefore comparable to the first published report from studies in Mongolia, but not subsequent reports from Singapore and the current study in Guangzhou.

Prevalence rates of PACG in Asian people have been reported from Beijing (rural),[21] Japan,[23] Tibet,[22] Taiwan,[7] Mongolia,[8] Singapore,[24] India (Andhra Pradesh),[174] India (The Vellore Eye Study).[175],and India in Madurai. The diagnostic criteria used in the in Beijing, Taiwan, Tibet, India (Vellore) studies did not specify GON as a requirement for the diagnosis of PACG. In contrast, the diagnostic criteria in Mongolia, Singapore, India (Andhra Pradesh) and the current study in Guangzhou are more comparable in this respect. The prevalence of occludable angles defined by gonioscopic findings has never been reported in mainland China, as gonioscopy was not uniformly conducted in any of population-based studies. The prevalence of PACS, PAC, PACG in those aged 40 years and over were found to be 6.4%, 2.0% and 0.8% in Mongolia, these rates in Singapore were reported to be very similar[176] The prevalence of

occludable angles and manifest PACG were reported to be 1.4% and 0.7% in an urban population (30+ years of age) of Andhra Pradesh, in South India. The findings in the current study were 10.2%, 2.4% and 1.5% in PACS, PAC and PACG in adult Chinese aged 50 years and over.

The variation in the prevalence rates may be explained by the variation of anatomical risk factors, such as anterior chamber depth. However, one study reported the overall distributions of axial ACD were very similar in Taiwanese Chinese, Caucasians and African American people in Baltimore.[77] The authors suggested that this finding indicated other anatomical or physiological characteristics may determine the risk of angle-closure in people of Chinese origin, such as "creeping" angle-closure and plateau iris.

In the current study, the prevalence of all categories of angle-closure were higher in women than men: PACS (2:1 F:M) and PAC (3:1 F:M) and PACG (1.6:1.3% F:M). Similar findings have been reported in other population data. There is some evidence this sex difference might be explained by some anatomical factors, primarily a shallower ACD in women Higher rates of PACS/PAC/PACG were also found in older subjects, again consistent with the previous finding of shallower axial ACD in older subjects.[20;25;28]

Among the cases of PAC and PACG, 38% had suffered a previous symptomatic episode, and about half had been diagnosed and treated prior to their identification in this study. The proportions of previous symptomatic PAC were reported as 25% in Mongolia[8], 43% in Singapore[24] and 35% in rural Taiwan.[7] These consistent findings suggest that a higher proportion of PAC and PACG cases experience a disease course without acute symptoms, and do not sustain destructive anterior segment sequelae. Identifying these asymptomatic, chronic PAC sufferers will be one of the major challenges in any effort to mount a preventive program.

4.1.5 Biometric characteristics in the population

Study of Greenland Inuit and Mongolians give an insight into the variation of ACD with age[25;28] in populations with a high risk of angle-closure. Both studies

identified three phases in ACD variation by age. In the first phase, from birth to 15 years, mean ACD increased with age and reaches a plateau at puberty. In the second phase after puberty, there is a relatively rapid decline in ACD with age was observed in both Eskimos and Mongolian people. The decline in ACD was most pronounced before the age of 40 in Eskimos and 60 years in Mongolians. In the last phase, the age-related decline in mean ACD continues, but is less pronounced.

In the elderly population, the change in ACD with age is believed to be determined by changes in lens thickness and position,[25;177] and hence these variables will interact with each other. This will affect the choice of statistical methods used to perform analyses. The choice of statistical method will also be influenced by the distribution of values (whether they are normally-distributed or not) and the relationship between age and ACD (linear or not). By examining histograms and Q-Q plots (comparing the quantiles of the observed variables and the expected quantiles in normal distribution), the distribution of ACD was found to be approximately Gaussian, while the lens thickness values were not, with disproportionately more observation in the extreme ends. The distribution of axial length was close to a normal distribution, although there was a slightly skew towards higher values (i.e. a right handed skew). These findings suggest that analysis using linear regression is probably valid for ACD and AL, but results for LT should be interpreted with caution. The LT data distribution is bimodal (Figure 25), being not consistent with data from Singapore where showing a typical unimodal Gaussian distribution. The alignment error in ultrasound measurement is unlikely given the other outcomes during ultrasound biometry, such as ACD and axial length, are all Gaussian distributed. The examination protocol requires achieve less than 0.13mm standard deviation for the ACD (readings with largest variation are dropped and repeat measurement), therefore, the variation due to handheld ultrasound could perhaps be minimized. The ultrasound was calibered and the gates settings were double checked every day before the examination. So the problems due to machine setting are less likely. Unfortunately, the problem of LT distribution was only able to realize during the phase of data anaysis, there is no explanation for this problem. Therefore, the data on lens thickness and relative lens position should be explained with caution, the medium and 25th and 75th percentiles are used to represent the

distribution and linear regression model is not used for the analysis.

Lowe used clinic-based data to compare the biometry in 61 subjects with angle-closure, with 80 normal control subjects. It is probably fair to assume that the affected cases had mainly presented with symptomatic angle-closure, although this is not clearly stated. For the "normal" subjects, the diagnostic criteria are not defined. Based on the findings of a 1.0mm shallower ACD and 0.6 mm thicker lens in the cases of angle-closure compared with the normals, he concluded 35% of the difference in ACD was attributable to lens thickening, and the remaining 65% was due to a more anteriorly positioned lens.[73;141] He also suggested that the relationship between ACD and axial length was less consistent in angle-closure eyes. Assuming the association of biometric indices with age is linear, we examined biometric data from all study subjects in Guangzhou, and compared people aged 50-59 with those 80+ years, the median ACD measured by ultrasound (including corneal thickness) decreased from 2.78 mm to 2.57mm, indicating the anterior surface of the lens was 0.21 mm closer to the cornea in the more elderly. The lens thickness was 0.37 mm thicker in older people suggesting the lens surface was 0.185 mm more anterior relative to the lens mid-point. The ACD difference minus ½[lens thickness] difference (0.21 – 0.185) was 0.025 mm. This suggests that between the 6th and 9th decades of life, only 12% of AC shallowing is attributable to anterior movement or positioning of the lens. Therefore, in the population of Guangzhou, the variation in ACD with age is largely attributable to changes in lens thickness, rather than changes in lens position.

In current study, the mean ACD measured by optical pachymetry was found to be shallower in older subjects, dropping from 2.61mm in 50-59 decade to 2.33 mm in the 80-93 age group. **Figure 54** compares mean ACD in various populations (all measured by optical pachymetry) and suggests the mean ACD in the population of Guangzhou is deeper than in Mongolia, and probably similar to the Singaporean Chinese population (**Figure 55**). Mean difference between men and women was 0.17 mm (M>F), and was similar to the 0.15mm found in Eskimos, 0.12mm in Mongolians and 0.17mm in Singaporeans.

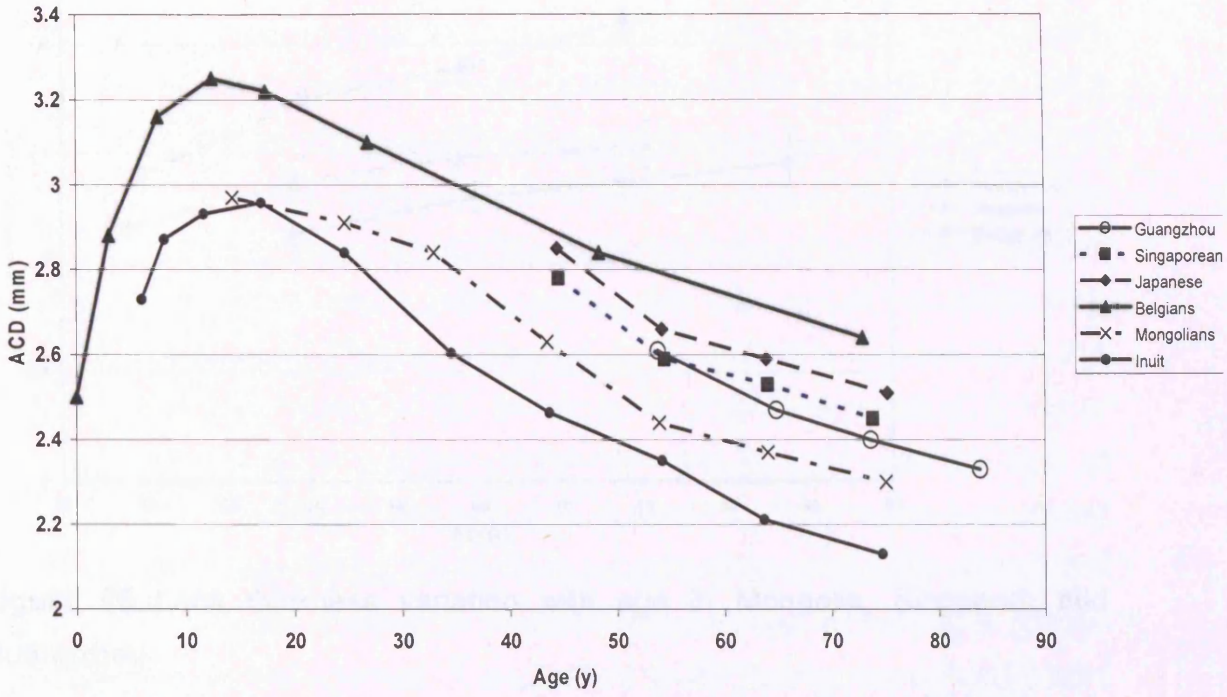


Figure 54 Inter-ethnic anterior chamber depth variation.

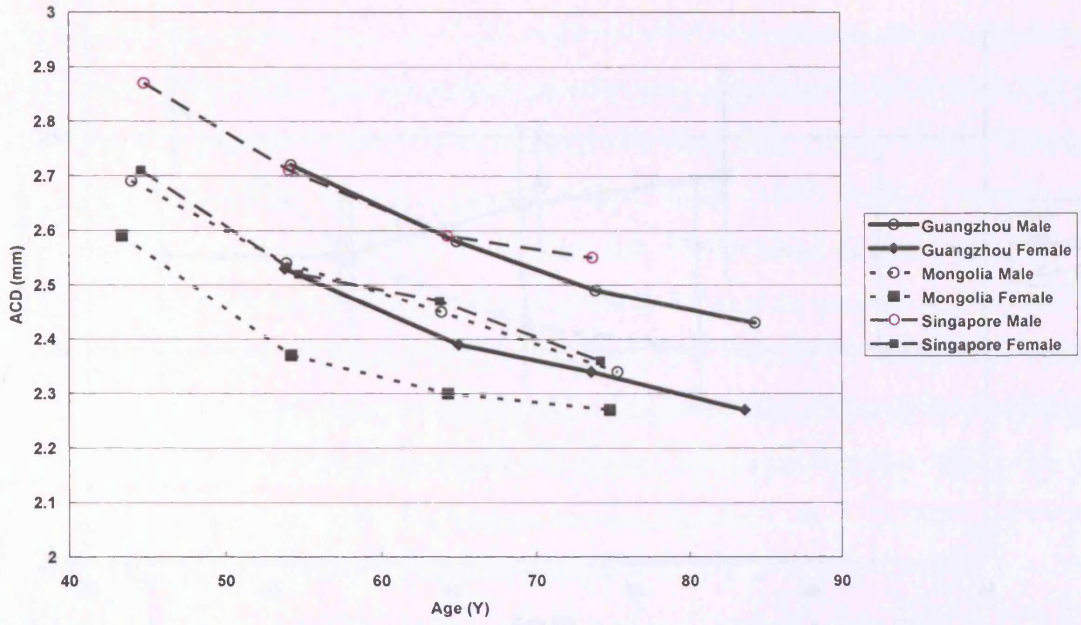


Figure 55 Anterior chamber depth variation with age by gender in Mongolia, Singapore and Guangzhou

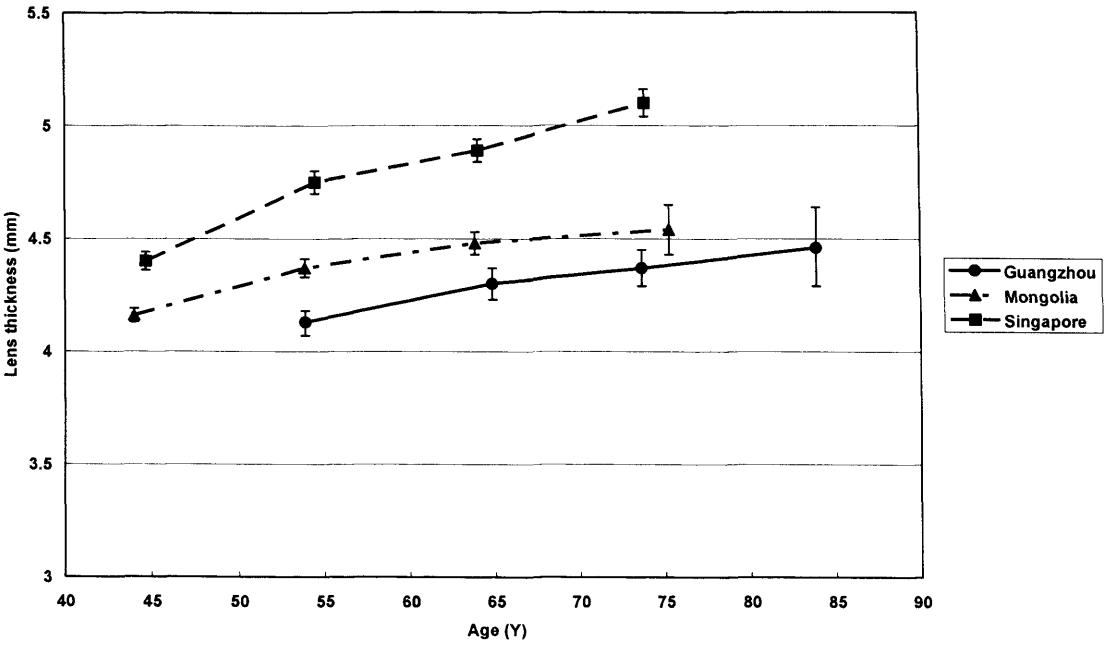


Figure 56 Lens thickness variation with age in Mongolia, Singapore and Guangzhou

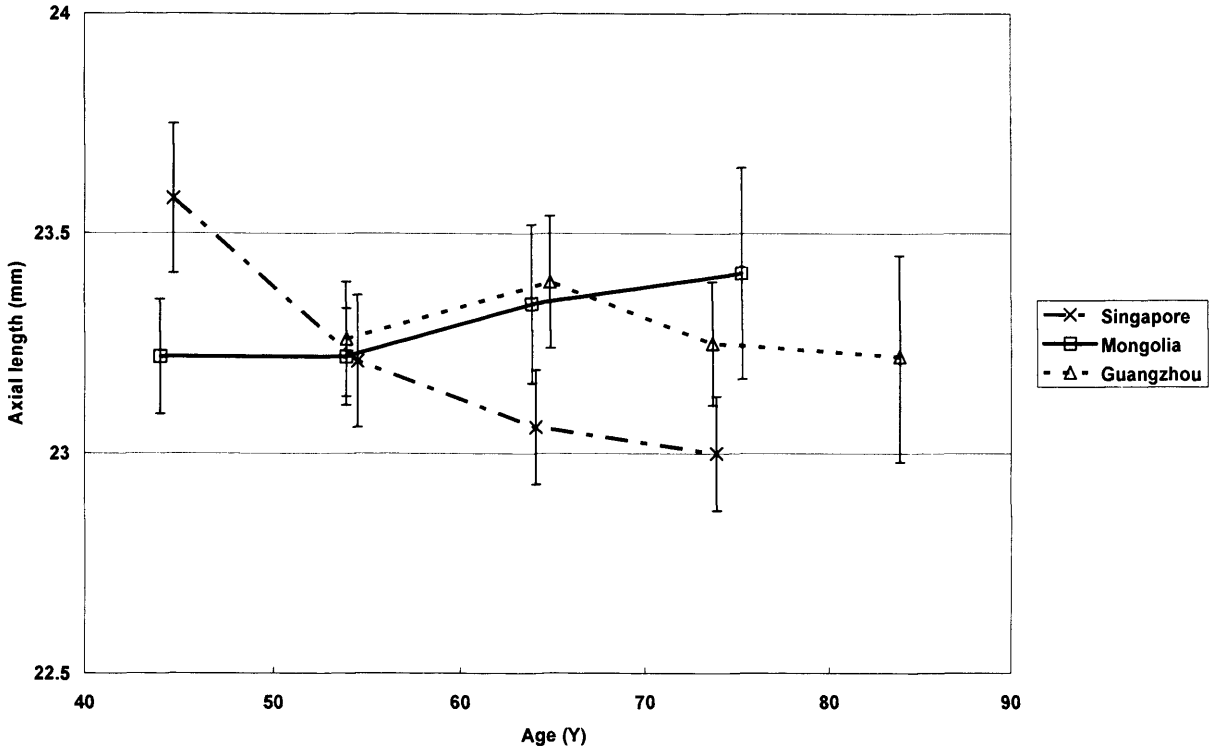


Figure 57 Axial length variation with age in Mongolia, Singapore and Guangzhou

Recently, there has been a growing recognition that there may be a "cohort effect" seen in ocular biometric parameters with age, related to the higher rate of myopia in the younger Asian people.[178;179] The observation that ACD decreases

with age appears common to all racial groups studied to date. The same pattern was seen in the present study. A plausible hypothesis is that the higher prevalence of myopia in younger people is attributable to longer axial lengths and deeper ACD's in younger people. To investigate this possibility, one must look at the distribution of axial length with age in these populations, to assess the possibility of a cohort effect related to myopia. **Figure 57** compares AL distribution by age in Singaporean Chinese, Mongolian and Guangzhou Chinese populations. The decrease in mean axial length with increasing age is only observed in Singapore. Neither Mongolian nor Guangzhou Chinese show the same significant decrease in AL with age. In Singapore, there is a higher prevalence of myopia in younger people, affecting 45% of men and 52% of women at 40-49, falling to 25% and 27% in those at 50-59 ages. This higher prevalence in younger cohort (40-49) may be associated with higher educational attainment in a more competitive environment, perhaps implicating a greater exposure to near work activity.[180] In contrast to the observations made in the Singaporean population, the mean AL in Mongolia and Guangzhou changes little with age. In our study population, most of subjects were born before the 1950s. At this time, when the majority of our patients should have received high school and college education, the education system was significantly weakened by the effects of the Japanese War (1938-1945), the Civil War (1945-1949), post-war recovery (1950-1960) and the Cultural Revolution (1966-1976). Therefore, it seems likely that the subjects in the current study were not exposed to the effects of an active, well-resourced, competitive education system. It may be that both Mongolian and Guangzhou populations are relatively untouched by the effects of an education-related effect driving higher rates of myopia (and longer axial dimensions) in younger people. Hence the decease in mean ACD with age (at least in Mongols and Chinese in Guangzhou) is probably genuinely age-related, without being subjected to other influence.

4.1.6 Association of biometric characteristics with angle closure

4.1.6.1 Gonioscopic characteristics of the drainage angle

Data on the gonioscopic appearance of the drainage angle was collected on all subjects in the current study, allowing geometric angle-width, trabecular pigmentation, iris profile and insertion, as well as changes in these variables after laser, to be examined.

Gonioscopy has been used and reported in the population studies in Framingham, USA [79], Mongolia,[8] Singapore,[24] a clinic-based study of Vietnamese subjects in California [82] and a mixed Cape-Malay population in South Africa [81]. Ethnic/racial differences are apparent. The percentage of narrow angles (Shaffer grade $\leq$ 2) was less than 5% in Europeans but nearly 50% in Vietnamese people.

Our work carried out in Guangzhou has the advantage of being population-based, therefore, giving a cross-sectional picture for the detailed gonioscopic characteristics in the community at large. As was the case in previous reports,[51;181] angle width was found to be narrowest in the superior quadrant. The widest angle was found in the inferior quadrant in the sitting position. This variation in angle width by quadrant was postulated to be artifact because of inadvertent indentation of the superior cornea.[52] Our UBM data seems to support this interpretation: both the superior and inferior quadrants have narrower angles compared with the nasal and temporal ones. The artifact induced by the indentation of eye cups on the limbus is less likely because the structure on interest is on the center of eye cup during the image acquisition when the patients are asked to gaze at the markers on the ceiling. These 4 markers used to direct the gaze are set up on the ceiling with an angle of about 20 degree between the measurement axial and gaze.

Comparable to the findings from other studies, we also found that the drainage angles were narrower in older people and women. Again, these characteristics in the width of drainage angle are in consistent with the findings in the higher

prevalence of PAC/PACG in older people and females.

Using the Spaeth grading system, the level of iris insertion can be assessed in two ways: "apparent" iris insertion on static gonioscopy and "true" iris insertion assessed by dynamic gonioscopy. Data from the current study suggests the proportion of apparent anterior insertions (Grade A and B) was low in men in their 50's, 5.4% in the superior and 1.5% in the inferior quadrant. This rate increases considerably to over 30% in superior and 9.1% in inferior quadrant in men in the 70-79 years. The proportion of Grades A and B in women is generally twice that in men. The variation in apparent iris insertion with age and sex was similar to the variation seen in angle width. The data on the level of true iris insertion tells a different story. In total, only 16 cases (right eyes) with true insertion Grade A (anterior to Schwalbe's line) and Grade B (behind Schwalbe's line) at superior quadrant and 6 cases (right eyes) with Grade A or B at inferior quadrant were seen. The cases with grade A or B "true" iris insertion, diagnosed using dynamic gonioscopy, all had PAS. The most common level of true iris insertion was Grade D (55.4% at superior and 70.8% at inferior quadrant). Because the proportion of Grade A or B was very small, it seems likely that the Grade C cases represented the most anterior level of true iris insertion. The proportion of Grade C insertions tended to be higher in older people, and was higher in women than men in all four quadrants. These findings are consistent with UBM measurement (distance from iris insertion to scleral spur) and would appear to be associated with the higher proportion of occludable angles in older and female subjects (a further, detailed discussion will be given in UBM section). More anterior iris insertion in older people may be an ageing effect, although biological mechanism is unknown. Sex differences are presumably a reflection of the differences between men and women observed in biometry.

A comparative gonioscopic study comparing the level of iris insertion in Caucasian and East Asian people[83] found 10%, 80% and 10% grade C, D and E insertions respectively in Caucasian people, and 27%, 69% and 4% for C, D and E grade in East Asian people. It is striking to find that the proportions of C, D and E insertions was very similar to our subjects in Guangzhou; 36%, 55% and 7% for grade C, D and E superiorly and 20%, 71% and 9% in the inferior quadrant). Comparison of these proportions with those seen in Caucasians seems to

suggest that East Asia people have a more anteriorly-located iris insertion. Oh et al therefore proposed the more anterior iris insertion explained the tendency toward "creeping" angle-closure in which synechiae form circumferentially and also creep anteriorly. But this theory, we believe, is speculative and needs to be proved in further longitudinal observations. UBM data in the current study provide an additional insight into the contribution of the anterior located iris insertion in angle-closure. An anterior iris insertion will enhance the peripheral crowding of the angle, as a consequence of a prominent last iris roll, a thick peripheral iris or an angulated, anteriorly-rotated iris insertion and tends to lead to appositional closure of the drainage angle (**Table 42**).

The clinical grading of iris profile used in the current study was adapted from the system proposed by Spaeth[181]. An additional grade "plateau" has been added to the original three categories: Steep (s), Regular (r) and Queer (q), or concave. In general, a "steep" iris profile is believed to be associated with relative pupil block. It was intriguing to find the proportion of iris profile differed according to age and gender. The proportion of "steep" iris profile increased with age, from 19% in 6th decade, 34% in 7th decade, 45% in 8th decade to 48% in 9th decade. Also, a higher proportion of steep iris profile was found in female subjects. It was also interesting to see the number of subjects with "queer" (concave) iris profile was very few- only 2.7%. These tended to be more common in younger people which perhaps associated with a higher prevalence of high myopia, although more evidence is needed to substantiate this hypothesis. The proportion of "plateau" iris was found to be quite stable with age, around 12% to 15% in all age groups, with slightly higher proportion in females. However, this observation must be interpreted with some caution, as the classification of "plateau" iris profile made using gonioscopy describes only the anterior surface of the iris. Without ultrasound examination, it is not possible to assess the anatomical characteristics posterior to the iris, and the hence the cause of angulation of the peripheral iris will remain unclear.

4.1.6.2 Association of biometric and gonioscopic angle narrowing

Table 21 summarizes risk factors for angle-closure, including anatomical, demographic and anthropometric characteristics associated with narrowing of

the drainage angles. Several well-recognized associations were found: shallower AC's, thicker lenses, shorter axial lengths, more anteriorly-located lenses and hyperopic refraction tended to be associated with narrower drainage angles.[25;178;182] The pattern of this association is similarly found in ACD. However, these associations are not invariable. Occludable angles can also occur in myopic eyes with relatively long axial lengths and deep AC's.[73] Other factors, such as iris thickness, location and angulation of the iris insertion probably also play a role in the narrowing of the drainage angle. The details will be discussed in UBM section.

PAS provide perhaps the best evidence that angle-closure has occurred. The rate of PAS in Shaffer grade 4 angles was 0%, increasing to 1.4% in grade 2, with further sharp increases to 12% in grade 1 and 28% in grade 0. This increasing trend with narrowing of the angle width suggested a dose-response effect between angle width and risk of closure.[172] When interpreting these finding, one has to be cautious that this data is derived from a cross-sectional study, with relatively small numbers. It is of course very difficult to differentiate between areas of atypical iris dysgenesis (congenital) and PAS (acquired). Only a prospective study could determine whether these structures are genuinely acquired, pathological phenomena, and if their presence reflects an increased risk of raised IOP and subsequent glaucomatous optic neuropathy.

4.2 Case control study

In order to investigate further the anatomical basis of angle-closure in this population, some of the subjects enrolled in our study in Liwan District, Guangzhou were enrolled in a study of sub-groups: angle-closure suspects and "normal" controls. Because it was not possible to enroll and perform the detailed examination for all subjects, 1 in 10 of "normal" subjects were enrolled by systematic sampling after exclusion of those people with established angle-closure, and those who met the criteria to be classified "angle-closure suspects". Using this approach, we intended to generate data on a control group who were representative of people without angle-closure in the general population.

The criterion used to identify angle-closure suspects in this study was that the pigmented TM should be visible for less than 180° (2 quadrants). This differs from the definition of an occludable angle used in previous population surveys [8;24;183;184] which used a more stringent definition of 3 quadrants or more of the posterior (usually pigmented) trabecular meshwork being hidden from view. This change was made following the finding that many subjects with "primary" PAS, do not meet the traditional (three quadrants hidden) definition of "occludable",[172] suggesting the definition is unduly strict. Those subjects with PAC or PACG (indicating established PAS or GON respectively) were excluded from this analysis.

4.2.1 Anterior segment characteristics in cases and controls

Right eye data were available for 194 cases and 122 control subjects meeting the enrollment criteria. The cases tended to be older, female and more hyperopic than controls. The mean IOP in the two groups were not statistically different. The findings are consistent with the observation that angles tend to be narrower in older people and women.

In contrast to findings of similarity of the mean IOP, the biometric characteristics of cases and controls groups were significantly different. ACD and axial length were shorter, lens thickness was greater and relative lens position was more anterior. However, radius of corneal curvature did not differ between the two groups. The mean ACD was found to be 2.09 mm in cases and 2.57 mm in controls, reflecting a 20% difference (0.46 mm). This difference is smaller than that given in Lowe's report (1mm difference)[185]. Similarly, a 10% difference (0.51 mm) difference was found in lens thickness and an almost 1 mm (0.94mm) difference was found in axial length. However, the absolute value of lens mid-point position (ACD + 1/2 lens thickness) was found to be 4.86 mm in case and 4.91 mm in controls by ultrasound biometry (difference = 0.05 mm). Assuming the shallower axial ACD is the consequence of a combination of an anterior located lens (0.05 mm) and a proportionally thicker lens (0.51/2 = 0.25 mm) in this population, lens thickness contributes 5 times more than anterior positioning of the lens to shallowing of axial anterior chamber depth. Lowe (1969) conceived relative lens position (RLP), as an index of the position of the lens

mid-point, while de-emphasizing inter-individual variation in ocular axial dimensions axial length is taken into account. Our study shows RLP was 0.209 (SD: 0.019) in cases and 0.214 (0.014) in controls, representing a 2% difference. A 9% difference (0.20 versus 0.22) in Caucasians[177] and 6% difference (0.192 versus 0.204) in Eskimos[186] and 4% difference in Singaporeans (0.21 in controls) [187] were reported previously. This difference may be attributable to relatively higher prevalence of myopia in our population. Consistent with previous quantitative descriptions, the corneal curvature in cases and controls groups are not significantly different.

Because the cases and controls groups were defined according to the number of quadrants of visible posterior TM, other gonioscopic characteristics, such as angle width, "true" level of iris insertion and iris profile are compared and provide additional information in the cases and controls groups. As expected, the mean of angle width in the controls, compared to the cases group, was 6 times and 3 times wider in superior and inferior quadrants respectively. The more obvious narrowing of the superior quadrant may be in part an artifact of the gonioscopic examination, [52;188] Considering "true" level of iris insertion, most of the eyes with narrow angles had grade C (88% in superior and 56% in inferior quadrant) and control eyes had predominantly grade D insertions (57% in superior and 77% in inferior quadrant), suggesting that both apparent and true iris insertion is more anterior in eyes with narrow angles.

4.2.2 Screening methods for identifying the occludable angles (cases group)

In our study, a selection of potential screening tests were performed on subjects in both case and controls groups. This allowed us assess the efficacy of these methods in the identification of people with narrow angles. It is logical, but as yet unproven, that early diagnosis of primary angle-closure benefits these patients. It has been shown that treatment by either surgical iridectomy or laser iridotomy is less effective if extensive PAS and GON damage have developed.[120;121] The ideal screening test would be relatively simple, non-invasive and with high sensitivity and specificity in the detection of angle-closure.

Studies of the performance of screening tests have been conducted in both clinic and community settings. However, the characteristics of the subjects enrolled in these two settings are likely to be different. Clinic-based studies may tend to enroll people with symptomatic PAC in which pupil block is presumably predominant. Population-based studies will probably enroll more subjects with less severe, earlier PAC. Control groups drawn from a community are more likely to be representative of the population as a whole. Therefore, test performance suggested by these two study designs will differ. The most appropriate method of assessing test performance will depend on the eventual purpose to which the test will be put. Our study mainly aims to evaluate the efficacy in the identification of people at risk in the community screening.

The performance of the oblique flashlight test (used to estimate anterior chamber depth) has been studied in Asia, Europe and North America.[21;22;189] However, this screening test was shown to have poor sensitivity (45%) in the detection of occludable angles in India [47]. In the present study, the sensitivity and specificity were 79% and 80% for the detection of occludable angles. This is impressive as the analysis excluded definite PAC and PACG cases. The area under ROC curve was 0.83. If including definite PAC and PACG cases, the sensitivity and specificity were both 80%. Van-Herick pointed out [45] that the flashlight method may be subject to misclassification in eyes with either plateau iris configuration or in the cases with central shallowing of the anterior chamber but with wide drainage angles. In the present study, the traditional method using a torchlight was compared with a test performed with an eyepiece measuring graticule and slit lamp. This was in an attempt to make the test more objective, by measuring the ratio of length of the shadow and corneal diameter. The underlying hypothesis was that the reported poor performance of the side-light test is chiefly a consequence of a simplistic grading scheme and failure to standardize the direction of torch light. The general performance of the slitlamp technique did improve slightly (but not significantly), the area under the ROC curve increased from 0.82 in traditional method to 0.89 with the slit lamp method. A shadow with a ratio of 0.20 (relative to corneal diameter) was found to have a sensitivity and specificity of 91% and 71% respectively.

The performance of optical and ultrasonic ACD measurement was also

evaluated. The sensitivity and specificity were all above 80%, comparable to figures reported in Mongolia[38], Greenland[78] and Taiwan[7]. The identified cut-off value was higher (2.27 mm) in the present study compared to Mongolia (2.22 mm) and Greenland (2.00 mm). This could be explained by age-specific mean ACD being shallower in both Mongolia and Greenland. Consistent with the findings in Mongolia, the handheld ultrasound method was found to be inferior to optical pachymetry in terms of the efficacy. Slit lamp mounted ultrasound method was not used in the present study.

Limbal chamber depth (LCD) was first proposed as a screening test by van-Herick in 1969.[45] The proposed 4 point grading scheme was found to be roughly equivalent to a five-point (Shaffer) gonioscopic classification scheme, and sensitivity of 82% and a specificity of 84% in identifying eyes with ACD $\leq$ 2.0 mm after examining 135 American patients of all ages (including 26 with "PACG").

Efficacy of LCD as a screening tool in angle-closure was reported in the population with different level of risk on angle-closure in Framingham,[79] Greenland,[76] India,[47] Taiwan, [7] and Mongolia.[46] The target characteristic specified in these various studies differed; ACD $\leq$ 2.00 mm in Framingham and Greenland, gonioscopic finding of "occludable" angles in India, a diagnosis of "PACG" (although not using the criteria of disc/field damage, but rather an IOP >18mmHg or positive dark-room prone provocative tests) in Taiwan. In Mongolia, the performance of the tests was examined in detection of three different disease stages: occludable angles, primary angle-closure and angle-closure glaucoma.

The method used to categorize LCD relative to peripheral corneal thickness (PCT) has been discussed previously. The traditional van-Herick method uses a 4-point grading system: grade 1 <1/4 PCT, grade 2 =1/4 PCT, grade 3 1/4~1/2PCT, grade 4 $\geq$ 1PCT. There are two potential methodological problems using this method: grade 2 represents LCD exactly = 1/4 PCT therefore the number ought, theoretically, to be small. Also, there is a gap between grade 3 and grade 4 (LCD between 1/2 to 1 PCT not being specified). In order to address these deficiencies, Alsbirk and Foster proposed a 7-point grading system to replace the traditional van-Herick test.[46] The scheme proposed the use of

percentage fractions 0%, 5%, 15%, 25%, 40%, 75% and >100%. Grades 0%, 5%, and 75% grades were added to the original grades. In an attempt to improve reproducibility, a set of standard photos were produced. Cockburn [190] attempted to estimate the LCD in a more precise fashion and proposed decimal fractions be used when estimating the limbal chamber depth. In these schemes, LCD was expressed as a fraction of PCT to the nearest 0.1. This method was tested in 509 optometric patients with the LCD ranging from 0.1 to 6.0 units (median and mode were 1.0). However, to attempt to grade LCD in 0.1 units of corneal thickness may not be practical even with x 25 magnification. In the current study, an eyepiece measuring graticule was used at 25 x magnification. A number of problems were encountered. These interfered with LCD estimation using this more refined grading at high magnification. Firstly, more elderly patients often found it difficult to fixate and maintain steady gaze. Secondly, variation in peripheral iris anatomy was encountered, leading to some uncertainty in allocation of a specific grade. Features associated with this variation included a prominent last iris roll, iris crypts and other surface irregularities. Another source of variability relates to the choice of positioning of the optical section when performing the grading. Variation in location of the limbus between individuals could degrade the performance of the test, and inter-observer variation in the choice of location at which the grading is performed may make results inconsistent.

A number of other factors may also have a bearing on the efficacy of the LCD test in the detection of gonioscopically occludable angles. If the examination is assumed to be precise, the mechanism of angle-closure may be important. In eyes affected by a predominantly non-pupil block mechanism, the anterior convexity of the mid-peripheral iris will be absent or reduced (depending on the amount of relative pupil-block). It is conceivable, but unproven, that this will influence the relationship between LCD and gonioscopic observations. Further investigation of the relationship between LCD and gonioscopy in eyes with various mechanisms may be needed. In the current study, the use of an eyepiece graticule did not improve performance of the test, compared with estimates made with reference to standard photos. However, this belief is difficult to substantiate without a direct, masked comparison in the same subjects.

Table 54 The efficacy of limbal chamber depth examination in detection of angle closure

	Framingham	Greenland	Australia	India	Taiwan	Mongolia		Guangzhou
Type of study	Clinic-based	Community	Clinic	Clinic	Community	Community		Community
Detection target*	ACD≤ 2.00 mm	ACD≤ 2.00mm	Gonioscopy	Gonioscopy	PACG	Gonioscopy	PACG	Gonioscopy
LCD/PCT cutoff†	≤ ¼	≤ ¼	≤ 0.2	< ¼	< ¼	≤ 25%	≤ 5%	≤ 25%
N	135	311	1113	96	562	1717		294 (189 cases, 105 controls)
Sensitivity	24/29 (83%)	51/56 (91%)	24/27 (89%)	13 / 21 (62%)	9/16 (56%)	139/140 (99%)	26/28 (91%)	178/185 (96%)
Specificity	89/106 (84%)	136/255 (53%)	3/1086 (99%)	67/75 (89%)	461/487 (95%)	1022/1560 (66%)	1564/1689 (93%)	76/108 (70.4%)

* Target of detection: ACD indicates anterior chamber depth; gonioscopy definitions are not uniform: pigmented trabecular meshwork not visible in 2 or more quadrants is used in India and Taiwan, in 3 or more in Mongolia and Guangzhou, PACG: primary angle closure with established glaucomatous optic neuropathy.

† LCD: limbus chamber depth; PCT: peripheral corneal thickness. Both LCD and PCT is indicated by proportions of limbus corneal thickness.

4.3 Ultrasound biomicroscopy findings

4.3.1Validity and reliability of UBM measurement

The reproducibility of both image acquisition and analysis was assessed using images from one eye of 34 subjects; 16 with narrow angles and 18 controls in an attempt to ensure a sufficient number of angle-closure subjects in the evaluation. The repeat image acquisition was conducted by two separate sessions. The examiner performed examination in all quadrants on each session. In this way, we intended to avoid the examiner repeating the acquisition of data from one specific quadrant, and possibly biasing the result. The same principle was adopted for image analysis; the grader was forced to identify the scleral spur in one image in two separate occasions, in a similar manner to that used for measurement of angle opening distances and angle recess area. As expected, the difference in measurements made from different images was greater, although not significant, than the difference in measurements made on the same image. This suggests that there is greater variability associated with image acquisition than during image analysis. This agrees with Urbak's reproducibility study.[191] For image acquisition, the variation in angle width tends to be greatest in the nasal quadrant (P=0.015 for AOD250 and P=0.026 for AOD500). This finding does not support the assumption in Gazzard's study in Singapore, in which the UBM reproducibility in the superior quadrant was assumed to poorer and, that the images were more difficult to obtain.[118]

4.3.2 UBM measurements in the population.

The current study, to our knowledge, is one of the first one to present detailed, quantitative data on a large number of normal and narrow angle subjects. A similar study in Singapore was conducted for the comparison of fellow eyes of acute episode and normal controls.[187] The UBM parameters in right eyes were selected for presentation in 119 people with narrow angles and 68 normal control individuals. In total, more than 60% of the eligible individuals attended for UBM examination. Although the older subjects tended to refuse this examination, the gender difference was not significantly different between attendees and absentees; the overall angle status (from gonioscopy) was also not significantly

different between the subjects undergoing the test and those who did not. This suggests the angle characteristics of those from whom UBM data were collected were in general similar to the target population.

Pavlin presented quantitative UBM data from 9 normal subjects (not having angle-closure)[57] that perhaps is the first available data on normal subjects in the West. The method of measurement in Pavlin's study was very similar that used in the current study. This permits comparison of the data between the two studies although small sample size (N=9) and unknown demographic features of the subjects may hinder a valid comparison. The AOD500 in the "normal" control subjects in Guangzhou was 0.152 mm, about half of that in Pavlin's study (mean=0.347mm). This difference in angle width between Chinese and European people is consistent with the difference suggested by the measurement of axial ACD. In fact, the mean of ACD in our population is 2.49 mm but in the Caucasian subjects in Pavlin study it was 3.128 mm. The iris thickness at 750 microns location in the Chinese subjects (mean= 0.445 mm in the superior quadrant) was thicker than in Pavlin's European subjects (mean= 0.372 mm at 500 microns location). Another study of UBM dark-light changes in Caucasians reports IT 500 microns in the dark as 0.367mm,[192] (very similar to Pavlin's results) and supports the empirical beliefs that Chinese have a thicker iris. This also agrees with anecdotal reports from observations during laser PI procedures.

As expected, the indices of angle width (AOD250, AOD500, ARA750) were correlated with each other, with Pearson correlation coefficients of 0.78 to 0.82. In the normal controls, the angle width was not correlated with the iris thickness although a significant association did exist in subjects with narrow angles (this will be described below). However, angle width was linearly associated with trabecular-ciliary process distance (TCPD). The longer distance between trabecular meshwork and ciliary process, the wider angle was found to be. The association of AOD500 to other biometric data (axial length, ACD, relative lens position, lens thickness) was very similar to the findings in gonioscopic angle width.

A similar pattern of association between gonioscopic and UBM angle width

measures with age and gender was found. The peripheral iris thickness was greater in men (mean=0.467, SD=0.011) than women (mean=0.432, SD=0.105) (P=0.03), but not associated with age (linear regression model, P=0.607). It is more intriguing that the curvature of iris was found to be steeper in women (radius: M: 7.56 mm; F: 5.63 mm, P=0.019 in the superior quadrant).

4.3.3 Characteristics of UBM analysis in angle-closure

The mean angle width in angle-closure suspects, either by AOD250, AOD500, ARA750, was found to be about half of that found in normal control subjects. This finding agrees with and complements the clinical findings from gonioscopy. The relevant anatomical UBM features of iris thickness, iris curvature, iris insertion position are therefore further investigated in order to try to explain the narrowing of the angle. Only by using UBM can these parameters be examined.

The mean iris thickness at 750, 1000 and 1500 microns from the scleral spur did not differ significantly between case and control groups. The mean of AOD500 in case group was 0.054 mm, slightly higher than the mean of 0.039 mm (P<0.001) in fellow eyes of those with acute PAC in Singapore.[118] The iris thickness was found to have a modest negative, linear correlation with the AOD500 (ß=-0.21, P<0.004, R^2=6%) in the case group. However, this association was not found in the normal control subjects.

The radius of curvature of the posterior surface of the iris was found to be smaller (more convex) in case group, suggesting the iris in narrow-angle eyes tends to be convex, suggesting pupil block was present in many cases.

The mean position of insertion of the iris, by quantitative analysis, was found to be more anterior in "case" group. A linear association is found between AOD500 and ss-ir (scleral spur and iris insertion distance) (ß=0.36, P<0.0001, R^2=31%). Based on the single linear regression model, nearly a third of the variation in AOD500 was explained by the variation of iris insertion location. The proportions of variation of AOD explainable by linear regression were found to be 6% in iris thickness and 13% in iris curvature. Therefore, when examining the relationship with a single variable, the variation in AOD500 was best explained by variation in

the position of the anterior insertion of the iris. In other words, an anteriorly-located iris insertion perhaps contributes the most to narrowing of the drainage angle in eyes with angle-closure.

Qualitative assessment of the drainage angle provides additional information in the comparison of the cases and controls. No statistically significant differences were found in the proportion of eyes with an anteriorly-rotated ciliary body in case and control groups (both about 60%). This is an intriguing finding. Traditionally, anterior rotation of the ciliary body is considered a unique finding in the eyes with plateau iris configuration.[96] However, our study suggested that this feature can be seen in many other eyes. This may suggest that it is only in the presence of other circumstances, such as the combination of ciliary rotation with an anterior insertion of the iris, a thick peripheral iris or a more anteriorly-rotated iris root that will result in closure of the drainage angle. Garudadri found a high rate of anteriorly-rotated ciliary bodies (41%) even in the eyes that can be opened by laser iridotomy (presumably without plateau iris).[126] This study again suggests the anterior rotation of the ciliary body is not a unique feature of eyes with plateau iris syndrome.

Another important finding in the qualitative analysis was the high proportion of appositional closure in both cases and controls groups seen on UBM. The proportions of appositional closure in each quadrant decreased in the order: superior, inferior, nasal and temporal. This order was found to be the same in cases and controls groups. The pattern of variation in appositional closure by quadrants was reported to be in exactly the same order in a recent UBM study of Japanese eyes.[193] In this Japanese study, prevalence of appositional closure in the dark was reported as 79% superior, 64% inferior, 33% nasal and 26% in the temporal quadrant. These rates are very similar to those seen in our study although the enrollment criteria for subjects were different: the subjects in the Japanese study were recruited from hospital clinics, and identified on the basis of <1/4 van Herick grade, after excluding people with PAS. Ishikawa reported a lower rate (56%) of appositional closure in 178 Caucasian eyes with Shaffer grade of 1 or 2.[58]

In our study, the proportions of appositional closure were as high as 78% in the

superior quadrant, 60% in the inferior quadrant and 25% (lowest) in the temporal quadrant. Wilensky and Ritch empirically proposed that the identification of appositional closure of the drainage angle is the key indicator for high risk of significant angle-closure, and was therefore an indication for prophylactic iridectomy/iridotomy.[194] Because UBM examination allows assessment of the drainage angle in dark conditions, it may be the best tool (currently) for identifying eyes with appositional closure. However, we find that, by UBM dark examination, over 80% of occludable angles are identified to have some kind of appositional closure.Longitudinal data suggests only about 10-20% will develop PAC damage in 5-10 years [105;106;108]. Therefore, appositional closure may not be a good indicator for differentiating the eyes with potential risk to develop PAC, at least within this time frame. Similarly, the high rate (44%) of appositional closure in the superior quadrant, even in the controls group, further supports this hypothesis.

However, one has to cautious when attempting to identify appositional closure using UBM images. The location of the trabecular meshwork on UBM images is determined by estimation rather than visibility (TM is usually presumably located on the back surface of the cornea at a distance of 500 microns to scleral spur).[62] Therefore, "appositional" closure identified by UBM may only suggest contact between the peripheral iris and the scleral-cornea coat rather than contact with trabecular meshwork. This problem will perhaps lead to an over-estimate the proportion of eyes with appositional closure.

Gorin described the gonioscopic features of the drainage angle in great detail[195] and postulated two kinds of closure: B-type (close from the bottom of drainage angle) and S-type (close starts from the Schwalbe's line). B-type closure is probably analogous to what was later named "creeping angle-closure" by Lowe, and is believed to be a mechanism responsible for angle-closure.[86] This theory had never been proven because, until the advent of UBM, it was not possible to view the structures posterior to the peripheral iris by gonioscopy. Our study suggests that B-type closure (at least appositional cases, if not synechial) is not uncommon. About one third of eyes with appositional angle-closure have a B-type pattern. This proportion is very similar to that reported in Japan where 1/3 of appositional closure started as B-type.[196] Empirical observation suggests that

B-type closure mainly develops in eyes with a more anterior insertion of the iris.[196] However, these features in appositional closure are not always analogous with synechial closure; the association or transition from the pattern of appositional closure to synechial closure deserves more longitudinal investigation.

4.4 Study of outcomes of laser iridotomy

4.4.1 General outcomes in occludable angle eyes

Laser peripheral iridotomy (LPI) is the standard first-line intervention for acute and chronic PAC.[197] It is believed to prevent a recurrence of acute episodes and to eliminate the risk of an acute attack in the fellow eye.[198-201] PI eliminates pupil block, allowing aqueous to bypass the pupillary region through the iridotomy in the peripheral iris. Consequently, the iris becomes flatter and the drainage angle becomes wider.[125]

However, performing prophylactic iridotomy on patients with occludable angles is controversial. There is limited evidence on which to assess the risk-benefit ratio of this intervention. Limited data on the natural history of angle-closure in Europeans,[105] Eskimos,[106] and Indians,[108] provides some insight but this is not sufficient to fully understand the risks, and relevant risk factors, for progression of occludable angles to PAC or PACG, particularly in Chinese eyes. None of these studies have been able to identify any anatomical features results in the development of either an acute episode or chronic PAC. The current understanding of the indications for iridotomy, such as appositional closure, are largely based on opinion rather than evidence.[194] About ten percent of the people aged 50 years and over were found to have occludable angles in our study. To screen, identify and provide prophylactic treatment for this large group of patients could be challenging and unrealistic, not to mention the potential for adverse events in the long-term resulting from potential side-effects of the LPI on lens and corneal endothelium.

Ideally, to understand this issue, a randomized trial is needed to give a detailed description of the incidence of angle-closure in the treated and untreated groups.

However, this type of clinical trial is challenging and practically difficult because it requires a large sample size and long-term follow up to detect the small difference and (relatively) low incidence of PAC,[120] detailed documentation of the complications, and take into account any changes in anterior segment configuration from other interventions, such as cataract surgery. Therefore, a logical starting point is to describe changes in the anterior segment before and after LPI in the eyes with occludable angles. The use of UBM technology provides the opportunity to gather detailed biometric data on angle width, iris thickness and insertion. One particular purpose of the present study was to describe the anterior segment configuration before and after LPI, in order to assess the contribution of pupil block and other mechanisms responsible for angle-closure. A major advantage of the present study is that subjects were enrolled from the community. Therefore, any findings should be broadly representative of the population as a whole.

Over 60% of eligible subjects aged 50 years and older received LPI treatment. The demographic and gonioscopic characteristics of those who did and did not attend for UBM examinations in these age groups were not different; suggesting the potential for response bias is minimal. There was, however, a very low response rate (10%) in those aged 80 years and over (a total 20 subjects). This was because of the refusal or lack of interest from older people to undergo further treatment on their eyes (as suggested by the questionnaires administered to refusing). This limits the extrapolation of the results to the very old.

Intraocular pressure was found to drop by almost 3 mm Hg after the laser PI treatment, without subsequent use of medication. A normalization of IOP (better control of IOP) has been recorded previously after laser PI in the early stages of PAC with elevated baseline IOP (if GON had not developed) in Europeans [101;198] and Asians.[120;123] Because all PAC and PACG cases have been excluded for the analysis in the present study, the fall in IOP after PI can not be explained by the decline in IOP in this group of subjects with established PAC and elevated baseline IOP. A decline in IOP in subjects with occludable angles with normal baseline IOP was also found in a study in Mongolia.[120] In cross-sectional data from Singapore, Foster found a lower IOP in those with wider drainage angles. It

was hypothesized that this may be the result of tension on the trabecular meshwork, keeping pores open and facilitating outflow.[202] This hypothesis is supported by evidence of a fall in IOP after cataract surgery[203] and pilocarpine treatment.[204] This, however, awaits verification in definitive studies. Another possibility to explain the decline of IOP is the use of IOP lowering medications. However, in this series of patients, except in about 10% of cases in whom IOP increased after laser (treated with topical carbonic anhydrase inhibitor (Trusopt, Merck&Co Ins, NJ, USA) and 0.5% Timolol) no other agents resulting in IOP lowering were given. The patients were re-examined after 2 week after the laser treatment. This period of time was intended to allow sufficient "wash out" time for IOP-lowering effects of the medications.

4.4.2 Biometric difference before and after laser iridotomy

Consistent with other studies,[118;200;205;206] the axial anterior chamber depth did not change after laser PI. There was, however, an average increase of 1.7 units in angle width (Shaffer grade) after laser PI. This increase is comparable to that found in the Mongolian population-based intervention study (median: 2 grades increase), [120] and more than in a study in fellow eyes of those suffering acute PAC (mean: 0.8 grades increase) [118]. This increase in angle width following laser PI would suggest a major contribution of pupil block to angle-closure in Chinese people. Assuming the fellow eyes of those with "acute" PAC (Gazzard's study) were high risk eyes and were probably more prone to pupil block, one would expect the change in angle width to be more pronounced than it was, in comparison with the figures from the current study, and from Mongolia. Observational bias and reproducibility issues should also be considered as another explanation for these findings. Shaffer gonioscopic grading is subjective, and could bias results toward a greater or lesser observed change. One might expect an un-masked observer to identify a larger change, and a masked observer, a smaller change. In Gazzard's study, the angle width graded by gonioscopy was found to be the narrowest in superior and inferior quadrants than nasal and temporal quadrants, contrary to the findings of other studies.[79;81;82] This inconsistency highlights the variation and potential bias of gonioscopy method. Furthermore, on a gonioscopic examination, it is difficult to miss the signs of iridotomy, and hence, all these observations could be subject to

some biases. Consequently, masked grading of UBM images is probably a superior study design.

As expected, the lens thickness and axial length did not change significantly after PI. These results suggests laser PI eliminates the pupil block, and flattens the mid-peripheral iris, opening the drainage angle. The other ocular biometric characteristics, including the thickness and location of the lens, did not change after PI either.

4.4.3 UBM features before and after iridotomy

UBM data provides further quantitative data supporting gonioscopic finding of a wider drainage angle after PI, and help to identify the factors determining the structural change of cross-sectional iris profile.[62;96] The latter feature cannot be examined using gonioscopy alone. Angle width is believed to increase in all quadrants, although variably, after PI. In the current study, the angle recess area was found to increase by 75%, which is consistent with the findings in another study in acute PAC in Singapore[118] and a study in Italy.[119] The most marked increase was found in the superior quadrant. This has not been reported before, and the explanation is unknown. As expected, iris was found to become flatter after PI, as has previously been reported in other studies.[118;119;125] Other features that were identified and have not been reported before, were the posterior movement of ciliary body and increasing iris thickness after PI. It is probable, but not certain, that these changes are the consequence of less tension on the posterior surface of iris when the pupil block mechanism is eradicated. An increase on the iris-lens contact supports the concept of a decrease in the tension of iris.[205]

4.4.4 Mechanism of angle-closure and the determinants of angle opening after laser iridotomy

Understanding the proportion of angle-closure cases and suspects in whom pupil-block is cardinal mechanism responsible for closure is of paramount importance from the public health perspective. Prophylactic laser iridotomy is effective only in the eyes where pupil-block is the predominant mechanism. No

simple and effective prophylactic treatment has been identified so far for eyes with a mainly non-pupil-block mechanism. Therefore, we assume that population screening and prophylactic treatment will only be viable when the majority of the narrow angles in the community are predominantly the result of a pupil-block mechanism.

About one-fifth of eyes remain "occludable" after treatment based on gonioscopy in our study. This appears to suggest about 20% of people with narrow-angles in the community have a non-pupil block mechanism causing angle-closure. In a hospital-based study, Wang reported the proportion of mechanisms identified in 126 Chinese PACG patients (a mixture of acute PAC 58 cases, chronic PAC 68 cases) based on the features of UBM, before and after iridotomy. The proportion of "pure" non-pupil block was 8%, a smaller proportion than in our study. The proportions of "pure" pupil-block and "mixed" mechanism disease were 38% and 55%.[100] The UBM features used in classifying the mechanisms included iris bombe, anterior iris insertion, increase in iris-lens contact, thickening of the peripheral iris and anterior rotation of the ciliary body. However, to draw a conclusion on the mechanism as a mixture of a number of anatomical feature is difficult, and may be unrealistic because of significant overlaps.

In the current study, the gonioscopic designation of an "occludable" angle after laser iridotomy was used to identify a non-pupil block mechanism. This definition is arbitrary rather than evidence-based, and is based on the view of the pigmented trabecular meshwork being obscured for 270 degrees of circumference or more. This definition was used to maintain consistency with those used to recruit the subjects, and with previous studies. Another alternative would have been to use provocative tests to identify cases of so-called "post-iridectomy angle closure".[207] In this study conducted in 1979, the rate of positive dark room-prone provocative tests (pressure rise of >/= 8 mm Hg) was 60% after iridotomy in people with early PAC with less than 120° PAS, compared with 12.5% in normal wide angle eyes. Much lower positive rates are reported in Caucasian eyes.[208] However, the predictive value of provocative tests was found to be unsatisfactory in Wilensky's longitudinal study, with problems largely from false positive tests, and unproven reproducibility.[105] The difficulties and risks of conducting provocative tests in the field conditions further limited their use in the

current study. The third alternative to define "closure" of drainage angle after laser PI is the existence of appositional closure, which ideally should be confirmed by UBM in dark. Among our study cohort, about 60% of the eyes still had appositional closure in at least one quadrant, even after laser PI, while this proportion was 95% before laser PI. Appositional closure was eradicated after laser PI in 50% of superior and inferior angles, and 60% of nasal and 80% of temporal quadrants. Gazzard reported 11 (20%) out of 54 fellow eyes (50 Chinese, 5 Malays, 1 unmeasurable) had at least one quadrant that was fully closed (defined by ARA=0) even after laser PI.[118] If using the same criteria (ARA=0), we had 10 (13%) of 72 eyes completely closed in at least one quadrant after laser PI. This proportion was 43% (31/72) before laser PI. Again, the qualitative criteria used to define "residual angle closure after laser PI" are always arbitrary, and probably hinder drawing a firm conclusion on the outcome after treatment. To confirm the success or failure of laser PI will need prospective follow-up on a long term basis.

The anatomical features that specifically identify eyes with angles that do not open with a patent iridotomy are not clear. Ultrasound biometry does not identify any features (including ACD) that explain this difference in response between eyes with angle-closure. This is not consistent with previous belief that eyes with non-pupil block (particularly those with plateau iris syndrome) will have a deeper anterior chambers.[94] Quantitative data from UBM suggests the eyes with non-pupil block tend to have a thicker, more anteriorly inserted irises, narrower drainage angles and relatively anteriorly-rotated ciliary bodies in comparison with angle that do open after iridotomy. We also documented that angulation of the iris insertion can and does occur in the absence of anterior rotation of the ciliary body, even in the presence of a patent iridotomy. One has been notice that the sampling error in the UBM image acquisition may also contribute to the variation on the size of ciliary body, iris insertion and angulation. .

The current study identified several eyes in which angles remained narrow after a patent iridotomy. However, owing to the cross-sectional nature of this work, it was not possible to identify anatomical features prospectively associated with a risk of developing either acute episodes or chronic PAS, although it is assumed that narrowing of the drainage angle is prerequisite for development of this

damage.[172;186] Neither was it possible to assess whether the risk of developing PAC in eyes with a predominantly non-pupil block mechanism decreases when the pupil block component is eliminated. A prospective long term follow up of these patients is required.

4.5 Conclusions

The data presented in this study consolidate and complement the current existing knowledge on the magnitude and clinical characteristics of glaucoma, the predisposing anatomical features and mechanism of angle-closure and efficacy of prophylactic treatment for primary angle-closure suspects in East Asian people. The recently proposed ISGEO classification system for glaucoma is used in our study that may help further improve the validity in the comparison with other studies. Ultrasound biomicroscopy (UBM) is used to describe the anatomical features related to angle-closure in a large number of subjects. Some findings are important and have only been sparsely or never reported.

The prevalence of primary angle-closure is comparable to the results from Singapore and Mongolia, but the prevalence of primary open angle glaucoma (POAG) is at least at the same level to primary angle-closure in the adult Chinese living in urban settings of mainland China. This finding contradicts the previous data from mainland China where POAG cases were only identified in people aged 40 years and younger. The improvement on examination methods, including gonioscopy for everyone and more careful evaluation of glaucomatous disc and field damage, in conjunction with uniform diagnostic criteria allow a more robust estimation of the prevalence of glaucoma. Furthermore, glaucoma was found to be the second leading cause of blindness, following unoperated cataract in this urban Chinese population.

Primary angle closure suspect (PACS) does occur in Chinese people at a high rate, similar to findings from Singapore and Mongolia. Over 10% of people aged 50 years and over are identified to have "occludable" angle. This highlights the needs and challenges for assessing the role of prophylactic treatment. Biometric and gonioscopic features are described in detail for both PACS cases and normal controls subjects. UBM results suggest that an anteriorly-located iris

insertion perhaps contributes the most to narrowing of the drainage angle. Anterior rotation of the ciliary body in angle-closure is not uncommon in "normal" eyes, suggesting this feature is not unique to angle-closure, and probably does not indicate with certainty the likely development of plateau iris. Appositional closure is found to be very common in PACS eyes, and therefore suggests that using this as an indicator of high risk of angle-closure, and an indication for prophylactic treatment may not be appropriate. UBM also documents and confirms that the closure starting from the bottom of drainage angle ("B-type") is common in appositional closure.

Laser peripheral iridotomy was found to be able to significantly widen the drainage angle as a whole, and did not deepen the axial anterior chamber depth (as expected). About 20% of PACS eyes with angles remaining "occludable" after this treatment suggests non-pupil block is the cardinal mechanism in about 20% of PACS in the community. A thicker, more anteriorly inserted iris, and a relatively anteriorly-rotated ciliary body are predisposing factors in non-pupil block angle-closure.

However, owning to the cross-sectional nature of this work, it is not possible to identify anatomical or physiological features associated prospectively with the risk of developing either an acute episode or chronic PAS. Neither is it possible to address whether the risk in eyes with predominantly non-pupil block decreases when the pupil block component is eliminated. This will require a long term follow up of this cohort of patients. Because laser PI is only performed in one randomly selected eye in our study, the untreated eye may allow a better understanding on the natural history of angle closure. Further work on a larger number of subjects with longer duration of follow-up is planned and deserves more intense effort. This may offer hope for defining characteristics of people at risk from angle-closure more precisely, and provide more robust evidence for prophylactic strategic in the prevention of a large proportion of glaucoma blindness in East Asian people.

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GUANGZHOU GLAUCOMA FOLLOW-UP STUDY 2003
SCREENING FORM 初步筛选检查表 (FORM 1)

Name:_____ **Phone:**_____ **Address:**_____

A:

RAC	STREET	HOUSE	PERSON	AGE	SEX	MONTH	DATE

EDU	OCCUPA	INCOME	WEIGHT	HEIGHT

Medical history 病史询问

1.High blood pressure No Yes
2.Diabetes No Yes
3.Glaucoma No Yes
If yes, specify _____
4. Glaucoma acute episode? No Yes
If yes, specify _____
5. Blood relatives have glaucoma? No Yes
If yes, specify relative(s)_____

B: REFRACTION 自动验光

Autorefraction (staple printout and record results)

	Sphere	Cylinder	Axis	R1	R2
OD					
OS					

Cannot be examined (reason) _____

C: VISION ASSESSMENT 视力检查

Habitual Visual Acuity 戴自用视远眼镜视力

	VA
OD	/
OS	/

Cannot be determined (reason): _____

D: Subjective refraction 主观视力(if PVA < 20/40)

	Sphere	Cylinder	Axis	VA
OD				/
OS				/

E: INTRAOCULAR PRESSURE 眼压

OD		mmHg
OS		mmHg

F:OPTICAL PACHYMETRY

	ACD	CT		Van-Herick	
OD			mm		CT
OS			mm		CT

G:Ultrasound biometry 超声测定

	AXIS	ACD	LT	VT
OD				
sd				
OS				
sd				

Cannot be determined (reason)_____

H: Ultrasound pachymetry 超声角膜测定

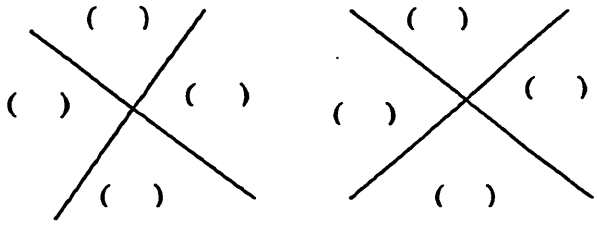
	THICKNESS	
OD		mm
OS		mm

I: GONIOSCOPY 房角镜

I1 Angular width

		0	10	20	30	≥ 40
OD	sup					
	Inf					
OS	sup					
	Inf					

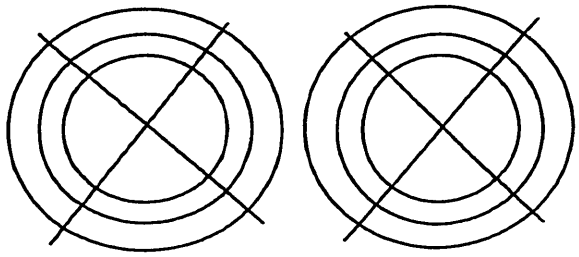
I2.Gonioscopy angle width (iris insertion)



I3. Iris Profile

	Steep	Regular	Queer	Plateau
OD				
OS				

I4 Goniogram under dynamic manipulation



OD OS

J: ENROLLMENT SELECTION ☐

1. Angle-closure suspect (include angle closure glaucoma)
2. 1 out of 10 normal control
3. Routine eye examination

GUANGZHOU GLAUCOMA FOLLOW-UP STUDY 2003
ROUTINE EXAMINATION 常规检查表

Name:_____ **Phone:**_____ **Address:**_____

H. Basic Eye Examinations 基本眼科检查

No abnormal findings ☐ ☐

Eyelid
- Defective closure ☐ ☐
- Inturned /trichiasis ☐ ☐
- Undertermined ☐ ☐

Globe
- **Ischaemic sequelae** ☐ ☐
- Pthisical ☐ ☐
- Conjunctivitis ☐ ☐
- Central corneal opacity ☐ ☐
- Trauma ☐ ☐
- Corneal ulcer ☐ ☐
- Pterygium ☐ ☐
- Others _____ ☐ ☐

Lens ☐ ☐
1. Normal – no opacity
2. Cataract- some red reflex
3. Cataract – no red reflex
4. Aphakia- no complication
5. Aphakia –with complication
6. Pseudophakia-no complication
7. Pseudophakia-with complication
8. Others _____

If it is cataract postop.cases

Date of surgery R____ L____ (YY/MM)

Hospital Name R_____ L_____

Type of cataract surgery ☐ ☐
1. ICCE
2. ICCE-AC IOL
3. ECCE
4. ECCE-AC IOL
5. ECCE-PC IOL
6. Phaco-PC IOL
7. Others _____

Incision ☐ ☐
1. Cornea
2. Cornea/scleral/limbal
3. Undetermined

Complications
- Eccentric pupil ☐ ☐
- Iris prolapse ☐ ☐
- Vitreous in AC/W ☐ ☐
- Corneal decompen. ☐ ☐
- After cataract ☐ ☐
- Pupil captured IOL ☐ ☐
- Subluxated IOL ☐ ☐
- Dislocated IOL ☐ ☐
- Uveitis ☐ ☐
- Others _____ ☐ ☐

I. Fundus 眼底检查
- Normal ☐ ☐
- Can not be seen ☐ ☐

If NOT normal mark all apply
- Congenital anomally ☐ ☐
- Optic atrophy ☐ ☐
- Glaucoma cupping ☐☐ ☐☐
- Maculopathy
  - ARMD ☐ ☐
  - High myopia ☐ ☐
  - Others ☐ ☐
  - Specify _____
- Retinochoriditis ☐ ☐
- Vascular
  - CRVO ☐ ☐
  - BRVO ☐ ☐
  - Arteriosclerosis ☐ ☐
  - Others ☐ ☐
- Diabetic retinopathy ☐ ☐
  - Stages_____
- Retinal detachment ☐ ☐
- Vitreous opacities ☐ ☐
  - Others_____
- Undetermined ☐ ☐

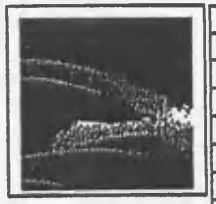
J. Principal cause for low vision/blindness
视力不良原因 (Presenting VA < 6/18)

Mark only one cause ☐ ☐
1. Refractive error
2. Cataract
3. Uncorrected aphakia
4. PCO/after cataract
5. Trachoma causing corneal scar
6. Xerophthalmia
7. Other corneal opacity _____
8. Pthitisical/disorganized/absent globe
9. Glaucoma
10. Optic atrophy
11. Vascular retinopathy
12. AMD
13. Amblyopia
14. Others _____
15. Undetermined

Appendix 2 Data collection forms for UBM measurement

Ciliary processes		Iris	Insertion	Iris Thickness		Iris convexity	Iris-TM contact	Mapstone Sinus
Size	Rotation	Position	Angulation	Basal	Overall	Absent		Not applicable
							None	Absent
Small	Neutral	Basal ✓	None ✓	Thin	Thin	Mild ✓		
							Low	Slit
Medium	Anterior	Mild	Mild	Medium ✓	Medium ✓	Moderate		
✓	✓						High ✓	Wide
Large		Apical	Pronounced	Thick	Thick	Extreme		

Name: 陈肖弟-12-30-1-OS-N rac: street: 12 house: 30 person: 1
eye: 2 quadrant: N LPI:



Professional 2000				
AOD250	AOD500	ss-ir	a	b
0	0	0.078	0.23	-93.38
ARA	TCPD	ICPD		
0.008				
Ubm xp				
AOD250	AOD500	IT500	IT1500	IFL
0	0	0.332	0.427	
AR-RA	TCPD	ICPD	AOD	
0.76	0.40	0.062	7.83	

Ciliary processes		Iris	Insertion	Iris Thickness		Iris convexity	Iris-TM contact	Mapstone Sinus
Size	Rotation	Position	Angulation	Basal	Overall	Absent		Not applicable ✓
							None	Absent
Small ✓	Neutral ✓	Basal ✓	None ✓	Thin ✓	Thin	Mild ✓		
							Low ✓	Slit
Medium	Anterior	Mild	Mild	Medium	Medium ✓	Moderate		
							High	Wide
Large		Apical	Pronounced	Thick	Thick	Extreme		

Name: 陈肖弟-12-30-1-OS-S rac: street: 12 house: 30 person: 1
eye: 2 quadrant: S LPI:

Professional 2000				
AOD250	AOD500	ss-ir	a	b
0	0	0.020	1.020	-89.89
ARA	TCPD	ICPD		
0.006				
Ubm xp				
AOD250	AOD500	IT500	IT1500	IFL
0	0	0.373	0.371	
AR-RA	TCPD	ICPD	AOD	
0.62	0.488	0.149	6.38	

Ciliary processes		Iris	Insertion	Iris Thickness		Iris convexity	Iris-TM contact	Mapstone Sinus
Size	Rotation	Position	Angulation	Basal	Overall	Absent		Not applicable ✓
							None	Absent
Small	Neutral	Basal ✓	None	Thin ✓	Thin	Mild ✓		
							Low ✓	Slit
Medium ✓	Anterior ✓	Mild	Mild ✓	Medium	Medium ✓	Moderate		
							High	Wide
Large		Apical	Pronounced	Thick	Thick	Extreme		

Name: 陈肖弟-12-30-1-OS-T rac: street: 12 house: 30 person: 1
eye: 2 quadrant: T LPI:

Professional 2000				
AOD250	AOD500	ss-ir	a	b
0.079	0.137	0.098	0.60	-124.70
ARA	TCPD	ICPD		
0.098				
Ubm xp				
AOD250	AOD500	IT500	IT1500	IFL
0.114	0.114	0.370	0.334	
AR-RA	TCPD	ICPD	AOD	
0.57	0.514	0.062	5.96	

GUANGZHOU GLAUCOMA FOLLOW-UP STUDY 2003
LASER IRIDOTOMY FOLLOW-UP (FORM 1)

Name:_____ **Phone:**_____ **Address:**_____

A:

RAC	STREET	HOUSE	PERSON	AGE	SEX	MONTH	DATE

B: REFRACTION 自动验光

Autorefraction (staple printout and record results)

	Sphere	Cylinder	Axis
OD			
OS			

Cannot be examined (reason) _____

C: VISION ASSESSMENT 视力检查

Habitual Visual Acuity 戴自用视远眼镜视力

Wearing glasses ? Yes ☐ No ☐

	VA
OD	/
OS	/

Cannot be determined (reason): _____

D: Subjective refraction 主观视力

(if PVA < 20/40)

	Sphere	Cylinder	Axis	VA
OD				/
OS				/

E: INTRAOCULAR PRESSURE 眼压

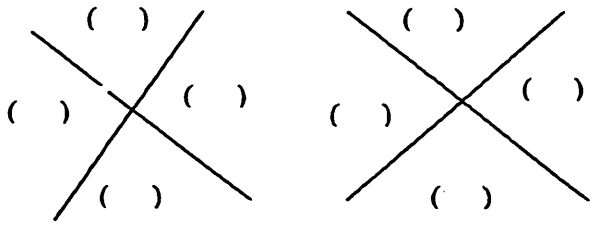
OD		mmHg
OS		mmHg

F: GONIOSCOPY 房角镜

F1 Angular width

		0	10	20	30	≥ 40
OD	sup					
	Inf					
OS	sup					
	Inf					

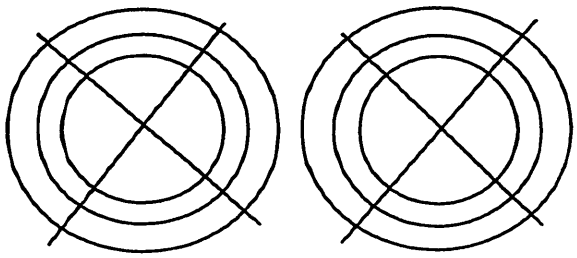
F2.Gonioscopy angle width (iris insertion)



F3. Iris Profile

	Steep	Regular	Queer	Plateau
OD				
OS				

F4 Goniogram under dynamic manipulation



OD OS

G: ENROLLMENT SELECTION ☐

1. Angle-closure suspect（include angle closure glaucoma）
2. 1 out of 10 normal control
3. Routine eye examination

Signature of Ophthalmologist _____

GUANGZHOU GLAUCOMA FOLLOW-UP STUDY 2003
ROUTINE EXAMINATION 常规检查表

Name:_____ **Phone:**_____ **Address:**_____

H. Basic Eye Examinations 基本眼科检查

No abnormal findings ☐ ☐

Eyelid

- Defective closure ☐ ☐
- Inturned /trichiasis ☐ ☐
- Undertermined ☐ ☐

Globe

- **Ischaemic sequelae** ☐ ☐
- Pthisical ☐ ☐
- Conjunctivitis ☐ ☐
- Central corneal opacity ☐ ☐
- Trauma ☐ ☐
- Corneal ulcer ☐ ☐
- Pterygium ☐ ☐
- Others _____ ☐ ☐

Lens ☐ ☐

1. Normal – no opacity
2. Cataract- some red reflex
3. Cataract – no red reflex
4. Aphakia- no complication
5. Aphakia –with complication
6. Pseudophakia-no complication
7. Pseudophakia-with complication
8. Others _____

If it is cataract postop.cases

Date of surgery R____ L____ (YY/MM)

Hospital Name R_____ L_____

Type of cataract surgery ☐ ☐

1. ICCE
2. ICCE-AC IOL
3. ECCE
4. ECCE-AC IOL
5. ECCE-PC IOL
6. Phaco-PC IOL
7. Others _____

Incision ☐ ☐

1. Cornea
2. Cornea/scleral/limbal
3. Undertermined

Complications

- Eccentric pupil ☐ ☐
- Iris prolapse ☐ ☐
- Vitreous in AC/W ☐ ☐
- Corneal decompen. ☐ ☐
- After cataract ☐ ☐
- Pupil captured IOL ☐ ☐
- Subluxated IOL ☐ ☐
- Dislocated IOL ☐ ☐
- Uveitis ☐ ☐
- Others _____ ☐ ☐

I. Fundus 眼底检查

- Normal ☐ ☐
- Can not be seen ☐ ☐

If NOT normal mark all apply

- Congenital anomally ☐ ☐
- Optic atrophy ☐ ☐
- Glaucoma cupping ☐ ☐
- Maculopathy
  - ARMD ☐ ☐
  - High myopia ☐ ☐
  - Others ☐ ☐
  - Specify _____
- Retinochoriditis ☐ ☐
- Vascular
  - CRVO ☐ ☐
  - BRVO ☐ ☐
  - Arteriosclerosis ☐ ☐
  - Others ☐ ☐
- Diabetic retinopathy ☐ ☐
  - Stages_____
- Retinal detachment ☐ ☐
- Vitreous opacities ☐ ☐
- Others_____ ☐ ☐
- Undertermined ☐ ☐

J. Principal cause for low vision/blindness
视力不良原因 (Presenting VA < 6/18)

Mark only one cause ☐ ☐

1. Refractive error
2. Cataract
3. Uncorrected aphakia
4. PCO/after cataract
5. Trachoma causing corneal scar
6. Xerophthalmia
7. Other corneal opacity _____
8. Pthithisical/disorganized/absent globe
9. Glaucoma
10. Optic atrophy
11. Vascular retinopathy
12. AMD
13. Amblyopia
14. others _____
15. Undertermined

GUANGZHOU GLAUCOMA FOLLOW-UP STUDY 2003

DEFINITIVE FORM 确诊检查表 (FORM2)

Name:_____**Phone:**_____**Address:**_____

A:

RAC	STREET	HOUSE	PERSON	AGE	SEX	MONTH	DATE

B. Medical history 病史询问

1.High blood pressure No Yes

2.Diabetes No Yes

3.Glaucoma No Yes

If yes, specify _____

4. Glaucoma acute episode? No Yes

If yes, specify _____

5. Blood relatives have glaucoma? No Yes

If yes, specify relative(s)_____

B: Flashlight Oblique Test 侧照法

By touch

	Narrow	Medium	Deep
OD			
OS			

By slit lamp graticule (Units)

	Shadow	Band
OD		
OS		

C: Limbus ACD 周边前房

By Standard photo

%	0	5	15	25	40	75	100
OD							
OS							

By graticule (Units)

	CT	Limbus ACD
OD		
OS		

D: OPTICAL PACHYMETRY

	ACD	CT	
OD			mm
OS			mm

E: Ultrasound biometry 超声测定

	AXIS	ACD	LT	VT
OD				
OS				

Cannot be determined (reason)_____

F:Ultrasound pachymetry 超声角膜测定

	THICKNESS	
OD		**Mm**
OS		mm

Cannot be determined (reason)_____

G. Appointment for UBM examination

Date: _____ (MM) _____(DD)

H. Eligible for laser iridotomy

No Yes

If Yes, appointment _____ (MM) ____(DD)

Signature of Examiner

_____

Appendix 4 Glossary of abbreviation

AACD	Axial anterior chamber depth
ACD	Anterior chamber depth
ALPI	Argon laser peripheral iridoplasty
AOD	Anterior opening distance
ARA	Anterior recess area
CT	Corneal thickness
CV	coefficient of variation
GON	Glaucomatous optic neuropathy
GSL	Goniosynechialysis
ICPD	Iris ciliary process distance
IOP	Intraocular pressure
LCD	Limbus anterior chamber depth
OCT	Optical coherence tomography
PAC	Primary angle closure
PACG	Primary angle closure glaucoma
PACS	Primary angle closure suspects
PAS	Peripheral anterior synechiae
PI	Peripheral iridotomy
POAG	Primary open angle glaucoma
SD	Standard deviation
SS-IR	Scleral spur iris root distance
TCPD	Trabecular ciliary process distance
TM	Trabecular meshwork
UBM	Ultrasound biomicroscopy